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Date of Deposit: March 5, 2001

# COMBINED DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and sole inventor of the subject matter (an original, first and joint inventor) which is claimed and for which a utility patent is sought on the invention entitled:

#### NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING THE SAME

the specification of which is attached hereto.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim the benefit under Title 35, United States Code, § 119(e) or §120 of any United States application(s), or §365(c) of any PCT International application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

Application No. (U.S.S.N.)	Filing Date (dd/mm/yy)	Status (Patented, Pending, Abandoned)
60/186,592	03/03/00	Pending
60/186,718	03/03/00	Pending
60/190,400	17/03/00	Pending
60/187,294	06/03/00	Pending
60/196,018	07/04/00	Pending
60/259,548	03/01/00	Pending
60/187,293	06/03/00	Pending

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Filed: March 5, 2001, herewith

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or patent issued thereon.

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### NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

#### RELATED APPLICATIONS

This application claims priority from USSN 60/186,592, filed March 3, 2000; USSN 60/186,718, filed March 3, 2000; USSN 60/187,293, filed March 6, 2000; USSN 60/187,294, filed March 6, 2000; USSN 60/190,400, filed March 17, 2000; USSN 60/196,018, filed April 7, 2000; USSN 60/259,548, filed January 3, 2001; each of which is incorporated by reference in its entirety.

#### BACKGROUND OF THE INVENTION

The invention relates generally to polynucleotides and polypeptides, as well as vectors, host cells, antibodies, and recombinant methods for producing these nucleic acids and polypeptides.

#### **SUMMARY OF THE INVENTION**

The invention is based in part upon the discovery of novel nucleic acid sequences encoding novel polypeptides. The disclosed FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6 and FCTR7 nucleic acids and polypeptides encoded therefrom, as well as derivatives, homologs, analogs and fragments thereof, will hereinafter be collectively designated as "FCTRX" nucleic acid or polypeptide sequences.

In one aspect, the invention provides an isolated FCTRX nucleic acid molecule encoding a FCTRX polypeptide that includes a nucleic acid sequence that has identity to the nucleic acids disclosed in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In some embodiments, the FCTRX nucleic acid molecule will hybridize under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule that includes a protein-coding sequence of a FCTRX nucleic acid sequence. The invention also includes an isolated nucleic acid that encodes a FCTRX polypeptide, or a fragment, homolog, analog or derivative thereof. For example, the nucleic acid can encode a polypeptide at least 80% identical to a polypeptide comprising the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The nucleic acid can be, for example, a genomic DNA fragment or a cDNA molecule that

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includes the nucleic acid sequence of any of SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Also included in the invention is an oligonucleotide, *e.g.*, an oligonucleotide which includes at least 6 contiguous nucleotides of a FCTRX nucleic acid (*e.g.*, SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24) or a complement of said oligonucleotide.

Also included in the invention are substantially purified FCTRX polypeptides (SEQ ID NO: 2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25). In certain embodiments, the FCTRX polypeptides include an amino acid sequence that is substantially identical to the amino acid sequence of a human FCTRX polypeptide.

The invention also features antibodies that immunoselectively-binds to FCTRX polypeptides, or fragments, homologs, analogs or derivatives thereof.

In another aspect, the invention includes pharmaceutical compositions that include therapeutically- or prophylactically-effective amounts of a therapeutic and a pharmaceutically-acceptable carrier. The therapeutic can be, *e.g.*, a FCTRX nucleic acid, a FCTRX polypeptide, or an antibody specific for a FCTRX polypeptide. In a further aspect, the invention includes, in one or more containers, a therapeutically- or prophylactically-effective amount of this pharmaceutical composition.

In a further aspect, the invention includes a method of producing a polypeptide by culturing a cell that includes a FCTRX nucleic acid, under conditions allowing for expression of the FCTRX polypeptide encoded by the DNA. If desired, the FCTRX polypeptide can then be recovered.

In another aspect, the invention includes a method of detecting the presence of a FCTRX polypeptide in a sample. In the method, a sample is contacted with a compound that selectively binds to the polypeptide under conditions allowing for formation of a complex between the polypeptide and the compound. The complex is detected, if present, thereby identifying the FCTRX polypeptide within the sample.

The invention also includes methods to identify specific cell or tissue types based on their expression of a FCTRX.

Also included in the invention is a method of detecting the presence of a FCTRX nucleic acid molecule in a sample by contacting the sample with a FCTRX nucleic acid probe or primer, and detecting whether the nucleic acid probe or primer bound to a FCTRX nucleic acid molecule in the sample.

In a further aspect, the invention provides a method for modulating the activity of a FCTRX polypeptide by contacting a cell sample that includes the FCTRX polypeptide with a

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compound that binds to the FCTRX polypeptide in an amount sufficient to modulate the activity of said polypeptide. The compound can be, *e.g.*, a small molecule, such as a nucleic acid, peptide, polypeptide, peptidomimetic, carbohydrate, lipid or other organic (carbon containing) or inorganic molecule, as further described herein.

Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, e.g., Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy lattice type I, and Reis-Bucklers corneal dystrophy. The Therapeutic can be, e.g., a FCTRX nucleic acid, a FCTRX polypeptide, or a FCTRX-specific antibody, or biologically-active derivatives or fragments thereof.

The invention further includes a method for screening for a modulator of disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast

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adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy lattice type I, and Reis-Bucklers corneal dystrophy. The method includes contacting a test compound with a FCTRX polypeptide and determining if the test compound binds to said FCTRX polypeptide. Binding of the test compound to the FCTRX polypeptide indicates the test compound is a modulator of activity, or of latency or predisposition to the aforementioned disorders or syndromes.

Also within the scope of the invention is a method for screening for a modulator of activity, or of latency or predisposition to an disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy,

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demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy lattice type I, and Reis-Bucklers corneal dystrophy by administering a test compound to a test animal at increased risk for the aforementioned disorders or syndromes. The test animal expresses a recombinant polypeptide encoded by a FCTRX nucleic acid. Expression or activity of FCTRX polypeptide is then measured in the test animal, as is expression or activity of the protein in a control animal which recombinantly-expresses FCTRX polypeptide and is not at increased risk for the disorder or syndrome. Next, the expression of FCTRX polypeptide in both the test animal and the control animal is compared. A change in the activity of FCTRX polypeptide in the test animal relative to the control animal indicates the test compound is a modulator of latency of the disorder or syndrome.

In yet another aspect, the invention includes a method for determining the presence of or predisposition to a disease associated with altered levels of a FCTRX polypeptide, a FCTRX nucleic acid, or both, in a subject (e.g., a human subject). The method includes measuring the amount of the FCTRX polypeptide in a test sample from the subject and comparing the amount of the polypeptide in the test sample to the amount of the FCTRX polypeptide present in a control sample. An alteration in the level of the FCTRX polypeptide in the test sample as compared to the control sample indicates the presence of or predisposition to a disease in the subject. Preferably, the predisposition includes, e.g., Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, e.g., Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell

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mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. Also, the expression levels of the new polypeptides of the invention can be used in a method to screen for various cancers as well as to determine the stage of cancers.

In a further aspect, the invention includes a method of treating or preventing a pathological condition associated with a disorder in a mammal by administering to the subject a FCTRX polypeptide, a FCTRX nucleic acid, or a FCTRX-specific antibody to a subject (e.g., a human subject), in an amount sufficient to alleviate or prevent the pathological condition. In preferred embodiments, the disorder, includes, e.g., Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, e.g., Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome,

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liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

In yet another aspect, the invention can be used in a method to identity the cellular receptors and downstream effectors of the invention by any one of a number of techniques commonly employed in the art. These include but are not limited to the two-hybrid system, affinity purification, co-precipitation with antibodies or other specific-interacting molecules.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

#### **DETAILED DESCRIPTION**

The invention is based, in part, upon the discovery of novel nucleic acid sequences that encode novel polypeptides. The novel nucleic acids and their encoded polypeptides are referred to individually as FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6, and FCTR7. The nucleic acids, and their encoded polypeptides, are collectively designated herein as "FCTRX".

The novel FCTRX nucleic acids of the invention include the nucleic acids whose sequences are provided in Tables 1A, 2A, 3A, 3C, 3E, 3F, 3G, 3H, 4A, 5A, 5C, 5E, 6A, 6C, and 7A inclusive ("Tables 1A - 7A"), or a fragment, derivative, analog or homolog thereof. The novel FCTRX proteins of the invention include the protein fragments whose sequences are provided in Tables 1B, 2B, 3B, 3I, 4B, 5B, 5D, 6B, 6D, and 7B inclusive ("Tables 1B - 7B"). The individual FCTRX nucleic acids and proteins are described below. Within the scope of this invention is a method of using these nucleic acids and peptides in the treatment or prevention of a disorder related to cell signaling or metabolic pathway modulation.

#### FCTR1

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Novel FCTR1 is a growth factor ("FCTR") protein related to follistatin-like gene, and mac25. FCTR1 (also referred to by proprietary accession number 58092213.0.36) is a full-length clone of 771 nucleotides, including the entire coding sequence of a 105 amino acid protein from nucleotides 438 to 753. The clone was originally obtained from thyroid gland, kidney, fetal kidney, and spleen tissues.

The nucleotide sequence of FCTR1 as presently determined is reported in Table 1A. The start and stop codons are bolded and the 5' and 3' untranslated regions are underlined.

### Table 1A. FCTR1 nucleotide sequence (SEQ ID NO:1).

The predicted amino acid sequence of FCTR1 protein corresponding to the foregoing nucleotide sequence is reported in Table 1B. FCTR1 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the cytoplasm (certainty=0.6500) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR1 protein is 11711.8 daltons.

### Table 1B. Encoded FCTR1 protein sequence (SEQ ID NO:2).

MASIEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTPDQLNSTGIPQLRSLNLVPEEEAESEENDDYY

FCTR1 was initially identified with a TblastN analysis of a proprietary sequence file for a follistatin-like probe or homolog which was run against the Genomic Daily Files made available by GenBank. A proprietary software program (GenScan<sup>TM</sup>) was used to further predict the nucleic acid sequence and the selection of exons. The resulting sequences were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length protein.

In an analysis of sequence databases, it was found, for example, that the FCTR1 nucleic acid sequence has 31/71 bases (43%) identical and 46/71 bases positively alike to a *Mus Musculus* IGFBP-like protein (TREMBL Accession Number:BAA21725) shown in Table 1C. In all BLAST alignments herein, the "E-value" or "Expect" value is a numeric indication of the probability that the aligned sequences could have achieved their similarity to the BLAST query

sequence by chance alone, within the database that was searched. For example, as shown in Table 1C, the probability that the subject ("Sbjct") retrieved from the FCTR1 BLAST analysis, in this case the *Mus Musculus* IGFBP-like protein, matched the Query FCTR1 sequence purely by chance is  $1.2 \times 10^{-11}$ .

### 5 Table 1C. BLASTP of FCTR1 against Mus Musculus IGFBP-like protein (SEQ ID NO:38)

PTNR:REMTREMBL-ACC:BAA21725 IGFBP-LIKE PROTEIN - MUS MUSCULUS (MOUSE), 270 AA. LENGTH = 270

10 SCORE = 161 (56.7 BITS), EXPECT = 1.2E-11, P = 1.2E-11 IDENTITIES = 31/71 (43%), POSITIVES = 46/71 (64%)

SBJCT: 191 EGLE-ELPGDHVNIAVQVRGGPSDHETTSWILINPLRKEDEGVYHCHAANAIGEAQSHGT 249

QUERY: 69 LTVLTPDQLNS 79 + | | | ++ |

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SBJCT: 250 VTVLDLNRYKS 260

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus Musculus* Follistatin-like Protein shown in Table 1D.

# Table 1D. BLASTP of FCTR1 against *Mus Musculus* Follistatin-like Protein (SEQ ID NO:39)

PTNR:SPTREMBL-ACC:Q61581 FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) - MUS MUSCULUS (MOUSE), 238 AA.

LENGTH = 238

SCORE = 149 (52.5 BITS), EXPECT = 1.5E-10, P = 1.5E-10 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* MAC25 protein shown in Table 1E.

### Table 1E. BLASTP of FCTR1 against Homo sapiens MAC25 protein (SEQ ID NO:40)

45
PTNR:SPTREMBL-ACC:Q07822 MAC25 PROTEIN - HOMO SAPIENS (HUMAN), 277 AA.

LENGTH = 277

SCORE = 149 (52.5 BITS), EXPECT = 3.2E-10, P = 3.2E-10 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

 The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus musculus* MAC25 protein shown in Table 1F.

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#### Table 1F. BLASTP of FCTR1 against Mus musculus MAC25 protein (SEQ ID NO:41)

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* Prostacyclin-stimulating factor shown in Table 1G.

# Table 1G. BLASTP of FCTR1 against *Homo sapiens* Prostacyclin-stimulating factor (SEQ ID NO:42)

```
PTNR:SPTREMBL-ACC:Q16270 PROSTACYCLIN-STIMULATING FACTOR - HOMO SAPIENS (HUMAN), 282

AA

LENGTH = 282

SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72

| | | | ++++ | | | | + + | | | | + | | | | + | | | + | | + | |

SBJCT: 209 LPGDRDNLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGQASASAKITVV 266
```

The amino acid sequence of FCTR1 also had 18/44 bases (40%) identical, and 25/44 bases (56%) positive for rat Colorectal cancer suppressor shown in Table 1H.

#### Table 1H. BLASTP of FCTR1 against rat Colorectal cancer suppressor (SEQ ID NO:43)

```
PTNR:PIR-ID:B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS)
40
                  LENGTH = 144
       SCORE = 78 (27.5 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
       IDENTITIES = 18/44 (40%), POSITIVES = 25/44 (56%)
45
      QUERY:
                33 FEVTGW--LQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTP 74
                           |+| | ||||||+|+| | ++ | | |
      SBJCT:
               101 FQIVGGSNLRILGVVKSDEGFYQCVAENEAGNAQSSAQLIVPKP 144
       SCORE = 37 (13.0 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
50
       IDENTITIES = 8/19 (42%), POSITIVES = 12/19 (63%)
      OUERY:
                 1 MASIEWRKDGLDIQL-PGD 18
                   + + + +
      SBJCT:
                30 MPTIHWOKNOODLTPNPGD 48
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The amino acid sequence of FCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive to bases 55-137, and 24/68 bases (35%) identical, and 37/68 bases (54%) positive to bases 166-225 of *Homo sapiens* PTPsigma-(Brain) Precursor shown in Table 1I.

## Table 1I. BLASTP of FCTR1 against Homo sapiens PTPsigma-(Brain) Precursor (SEQ ID NO:44)

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SBJCT:

QUERY:

SBJCT:

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PTNR:TREMBLNEW-ACC:AAD09360 PTPSIGMA-(BRAIN) PRECURSOR - HOMO SAPIENS (HUMAN), 1502
                                                LENGTH = 1502
       10
                       SCORE = 109 (38.4 BITS), EXPECT = 0.00010, P = 0.00010
                       IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)
                                            14 QLPGDD-PHISVQFRG---GPQRFEVTGW------LQIQAVR-PSDEGTYRCLARNALG 61
                     QUERY:
       15
                                                                                                    | | | | +
                                                                                                                                      |+|| +| | || | |+|+|++|
                                            55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLRIQPLRTPRDENVYECVAQNSVG 114
                     SBJCT:
                                            62 QVEAPASLTVLTPDQLNSTGIPQL 85
                     QUERY:
                                                               | | | | | | | +
      20
                     SBJCT:
                                         115 EITVHAKLTVLREDQLPS-GFPNI 137
                       SCORE = 77 (27.1 BITS), EXPECT = 0.25, P = 0.22
Ç.Ş
                       IDENTITIES = 24/68 (35%), POSITIVES = 37/68 (54%)
Hard grade glock strate that He's
       25
                                               4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALG-Q 62
                     QUERY:
                                                                                    +| ||++
                                                                                                                                                      + | + | | | + | + | +
                                                    | | | | +
                     SBJCT:
                                         166 ITWFKDFLPV-----DPSAS---NGRIKQLR-SGALQIESSEETDQGKYECVATNSAGVR 216
                     QUERY:
                                            63 VEAPASLTV 71
, 15 mm, 
      30
                                                        + | | + | |
                     SBJCT:
                                          217 YSSPANLYV 225
                                    The amino acid sequence of FCTR1 also had 32/83 bases (38%) identical, and 45/83
I THE HITTA GENERAL STREET
                     bases (54%) positive for amino acids 55-137 and 26/69 bases (37%) identical, and 38/69 (54%)
       35
                     positive for amino acids 166-234 of Homo sapiens Protein-Tyrosine Phosphatase Sigma shown
                     in Table 1J.
                      Table 1J. BLASTP of FCTR1 against Homo sapiens PTPsigma-(Brain) Precursor (SEQ ID
                                                                                                                 NO:45)
                     PTNR:SPTREMBL-ACC:Q13332 PROTEIN-TYROSINE PHOSPHATASE, RECEPTOR-TYPE, S PRECURSOR (EC
       40
                     3.1.3.48) (PROTEIN-TYROSINE PHOSPHATASE SIGMA) (R-PTP-SIGMA) (PTPRS) - HOMO SAPIENS
                      (HUMAN), 1948 AA.
                     LENGTH = 1948
                       SCORE = 109 (38.4 BITS), EXPECT = 0.00013, P = 0.00013
       45
                       IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)
                     QUERY:
                                            14 QLPGDD-PHISVQFRG---GPQRFEVTGW------LQIQAVR-PSDEGTYRCLARNALG 61
                                                                                                                                       + + + | |
                                                                  ++
                                                                                   +
```

55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLRIQPLRTPRDENVYECVAQNSVG 114

62 QVEAPASLTVLTPDQLNSTGIPQL 85 | | | | | | +

115 EITVHAKLTVLREDQLPS-GFPNI 137

SCORE = 88 (31.0 BITS), EXPECT = 0.023, P = 0.022IDENTITIES = 26/69 (37%), POSITIVES = 38/69 (55%)

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A ClustalW analysis comparing the protein of the invention with related protein sequences is given in Table 1K, with FCTR1 shown on line 2. In the ClustalW alignment of the FCTR1 protein, as well as all other ClustalW analyses herein, the black outlined amino acid residues indicate regions of conserved sequence (*i.e.*, regions that may be required to preserve structural or functional properties), whereas non-highlighted amino acid residues are less conserved and can potentially be mutated to a much broader extent without altering protein structure or function.

### Table 1K. ClustalW Analysis of FCTR1

```
1)
                        007822 MAC25 PROTEIN. (SEQ ID NO:40)
                        Q16270 PROSTACYCLIN-STIMULATING FACTOR. (SEQ ID NO:42)
              2)
W. 11.05
                        3)Q61581_FOLLISTATIN-LIKE 2: FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) (SEQ
    20
                                  ID NO:39)
                        BAA21725 IGFBP-LIKE PROTEIN (SEQ ID NO:38)
£13
              4)
                        FCTR1 (SEQ ID NO:2)
              5)
£.,}
                        B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS) (SEQ ID NO:43)
              6)
<u>1</u> ≥ 25
                                   mer<mark>as</mark>lrall<mark>fgp</mark>agllllllplssssssd<mark>t</mark>cgpc<mark>epas</mark>cpplpp<mark>lgcllget</mark>rd<mark>a</mark>cgc
              Q07822
fii
                                   mer<mark>ps</mark>lralllg<mark>a</mark>agllllllplssssssd<mark>tcgpc</mark>epascpplpp<mark>lgcllget</mark>rd
              Q16270
ti)
                                   MERP PRALLLGAAGLLLLLLPLSSSSSSDACGR
              Q61581
                                                                          RRHPECSPCQQDRCPAPSPCPAPWISARDECGCC
                                   MPRLPILLLL PSLÄRGLGLRDAG
              BAA21725
Tag
Tag
    30
              FCTR1
              B40098
L
Man H
                                   PMCARGEGEPCGGGGAGRGYCAPGMECVKSRKRR
PMCARGEGEPCGGGGAGRGYCAPGMECVKSRKRR
                                                                                        GKAGAAAGGPEVSGVCVCKSRV
              Q07822
The state of
                                                                                        GKAGAAAGGP VSGVCVCKSRYPVC
              Q16270
    35
                                                             RG<mark>H</mark>CAPGMECVKSRKRR
                                                                                         GKAGAAAGGP<mark>ATLA</mark>VCVCKSRYPVC
              Q61581
              BAA21725
                                                        GPVGSRC PG VCA SR
                                                                                          ASCTAPEC
                                                                                                         T GLCVCAQRGAVC
              FCTR1
                                                                                                             PLRFLSQTESIT
              B40098
     40
                                   gsdgttypsgcqlraas<mark>q</mark>raesrgek<mark>a</mark>
gsdgttypsgcqlraas<mark>q</mark>raesrgek<mark>a</mark>
                                                                                 ITQVSKGTCEQGPSIVTPPKDIWNVTGAQV
              Q07822
                                                                                 ITQVSKGTCEQGPSIVTPPKDIWNVTGAQV
              Q16270
                                    GS<mark>N</mark>G<mark>I</mark>TYPSGCQLRAAS<mark>L</mark>RAESRGEK<mark>P</mark>
                                                                                 ITQVSKGTCEQGPSIVTPPKDIWNVTGA<mark>K</mark>V
              Q61581
                                                                                 HKARDGPCEFAPVWMPPRDIHNVTG
              BAA21725
                                    GSDGRSYSSICALRLRARHAPRAHHGH
              FCTR1
     45
                                   AFMGDTVLLKCE I GDPMPTIHWQKNQQDLTPNPGDSRVVVP WFINHPSN WAYESMDI
              B40098
                                   LSCEVIGIPTPVLIWNKVKRGHYGVQRTELLPGDRENLAIQTRGGPEKHEVTGWVLWSP
YLSCEVIGIPTPVLIWNKVKRGHYGVQRTELLPGDRENLAIQTRGGPEKHEVTGWVLWSP
BLSCEVIGIPTPVLIWNKVKRDHSGVQRTELLPGDRENLAIQTRGGPEKHEVTGWVLWSP
BLSCEVKAVPTPVITWKKVKHSPEGTEGLEELPGDHVNIAYQVRGGPSDHETISWELLWP
MASJEWRKDGLDIO...LPGDDPHTSVQFRGGPQRFEVTGWJQTQA
EFECAVSCKEVPTVNWKKNGDVVV...ISDYFQIVGGSN...RTLG
              Q07822
              Q16270
              Q61581
     50
              BAA21725
              FCTR1
              B40098
              Q07822
                                   LSKED<mark>A</mark>GEYECHASNSQGQASASAKITVVDALHEI<mark>AS.....</mark>
     55
                                   lskedageyechasnsogoasasakitvvdalhei<mark>py.....kk</mark>gegæ
              Q16270
                                    lsked<mark>ageyechasnsqgqasa</mark>akitvvdalhei<mark>pb......kkge</mark>gaq
              Q61581
                                    LRKEDEGVYHCHAANAIGEAQSHGTVTVLDLNRYKSI......YSSVPGD
VRPSDEGTYROLARNALGOVEAPASLTVLTPDQLNSTGIPQLRSLNLVPEEEAESE<mark>E</mark>NDD
              BAA21725
              FCTR1
                                                             GNAQSSAQLIVPKP.....
              B40098
     60
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IGFBP is expressed in neurostem cell and developing central nervous system. MAC-25, a follistatin like protein is a growth suppressor of osteosarcoma cells, and meningiomas. DCC is expressed in most normal tissues especially in colonic mucosa, but is deleted in colorectal cancers.

Since FCTR1 has similarity to these proteins (shown in BlastP, Tables 1C-1J, and in clustalW, Table 1K) it is likely that it has similar function. Therefore FCTR1 could function as on or more of the following: a tumor suppressor geneor regulator of neurological system development.

Based on the protein similarity and tissue expression, FCTR1 may be useful in the following diseases and uses:

- (i) Tissue regeneration in vitro and in vivo
- (ii) Neurological disorders, neurodegenerative disorders, nerve trauma
- (iii) Reproductive health
- (iv) Immunological disorders, allergy and infection
- (v) In cancer as a diagnostic and prognostic marker, as well as a protein therapeutic

#### FCTR2

FCTR2 (alternatively referred to herein as AC012614\_1.0.123), is a growth factor bearing sequence similarity to human KIAA1061 protein and to genes involved in neuronal development and reproductive physiology (e.g., cell adhesion molecules, follistatin, roundabout and frazzled). FCTR2 is a full-length clone of 5502 nucleotides, including the entire coding sequence of a 815 amino acid protein. This sequence is expressed in glioma, osteoblast, other cancer cells, lung carcinoma, small intestine (This sequence maps to Unigene Hs.123420 which is expressed in brain, breast, kidney, pancreas, pooled tissue).

A FCTR2 ORF begins with an ATG initiation codon at nucleotides 420-422 and ends with a TGA codon at nucleotides 2865-2867. Putative untranslated regions upstream from the initiation codon and downstream from the termination codon are underlined in Table 2A, and the start and stop codons are in bold letters.

### Table 2A. FCTR2 Nucleotide Sequence (SEQ ID NO:3).

CAATTTCACACAGGAAACAGCTATGCCATGATTACGCAAGTTGGTACCGAGCTCGGATCCACTAGTAACGGCCGCCAGTG
TGCTGGAATTCGGCTTACTCACTATAGGGCTCGAGCGGCTGCCCGGGCAGGTCATTAATTCCATTTCTTTTTAGAGTATC
ACAGCTTTCTCCTTCACTGACCACCCCTTTGCTTCCTGTCAGAAAGCCCTTGGACAGAACTCTCTGTGGGATTCTGCCCATG

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TTTCTGAGATATCGCCTCAATTGTCCTGGCTGGGCTGTCGGGTCTGCCCGTTTTACAGATGGGCAAACTGGAGTGGGAAG TATCCGGGTGGCTTCCTCAGGCCTGCAGCTGGTGGAGCAGCTACTGAAACAATCAGGAGCCCAGAAGCTTTGAAGTCACA GCTGCCCTGACCTCTTTGGGCTTTCCAGCCGCAACGAGCTGCTGCCTCCTGCGGGAAGAAGTTCTGCAGCCGAGGGAGC 5 CGGTGCGTGCTCAGCAGGAAGACAGGGGAGCCCGAATGCCAGTGCCTGGAGGCATGCAGGCCCAGCTACGTGCCTGTGTG CGGCTCTGATGGGAGGTTTTATGAAAACCACTGTAAGCTCCACCGTGCTGCTTGCCTCCTGGGAAAGAGGATCACCGTCA  $\tt CTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGACAAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGGAATC$ 10  ${\tt ACCTGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACAGTGACAGCTCCCTGACC}$ CGTGGGGCTGAGCACAGTGCTGACCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGCTCA CACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGCTGTTCCAGACCCACGTCCTGCAGGTGAATGTGCCGCC 15 AGTCATCCGTGTCTATCCAGAGAGCCAGGCACAGGAGCCTGGAGTGGCAGCCTAAGATGCCATGCTGAGGGCATTC GGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAGGGGCATACACCTGCATTGCCAAAAATGAAGTGGGTGT 20 CACCTCAAACCCACGGAAAAGATTTTCATGAGCTATGAAGAAAATCTGTCCTCAAAGAGAAAAAAATGCAACCCAGCCCTG ACATCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCTATGACAAGTCACATGAC GAGCCAGCACCTCATCCGCACACCCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACA 25 TCAGGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAATGATGCCCCTCAAGACC TAACAGGCACCCCACACACCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCCCCTGGCTGCACGTGCAG GAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGCAAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCG 30 CTCCTTCACTGAAAGCAATCAATACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCCTGGAGCTGTCCA CGGGGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGCAGGGCCAGCTCAGCCCTGGGGGGGTACCCACAGAATC  ${\tt ATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAGCCCGAGAGTCACTGTTCCTCATCAATGGGAGACAAAA}$ GAGCCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTACATTTTTACAGACAAAAG 35 CAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTGCAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGA TTGGGGTTTTTTCGTTAGGAAGTATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTT <u>CTGTGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCAAGCAGACACCTCTGTCA</u> <u>CGACCAGGAGCAGGGGCCTCCCTCCCGAACTGAAAGCCCATCCGTCCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTG</u> 40 CTTCTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTGCATCTTGGGGGATGGGG TCCGAGGTCCAACTATATCCTTCCCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCCACATCCCACAGCCAGAAAG AACAATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCTGCTTCTCCAAGAGCAGACCAGGCCACCTCATCC GTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAAACCAGAACAAGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACA 45 TCTCATTAGTCAGGTCTGGTACCCCAGATTCAGGGCAGACTGGGCTTGCCTGGCAAGGTATGGGTGGCCTCCAGGCTCAA TGCAGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAACAGATTTTGTTTTCCTAC CTGTGGCCCATCCACTCCTCTGGTACCCCATCCCGCATCAGCACTGCAGAGAGAACACATTTCGGCGAGGGTTTTCT TACCCACATTCCCCAATCAATACACACACACCTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCT TATGTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCTCTGGAGACCGCCTAGAT 50 <u>CAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCCACATATGAGTGGAACTTACATGTGTCCTGGTTTGAATGATCA</u> TTTTGCAAGCCACACGGGTTGGGAGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACAT <u>GACCAGGATTTTCCTTTGCCATTAAGGAATGAACTCTTTCAAGGAGAGGAAACCCTAGACTCTGTGTCACTCTCAACACA</u> GTCTCACGCAACTTGGTCCACCAAACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTA 55 TTTTAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAGTTTCACAGTAGCTGGGA <u>TGCATGGATGACCCATCTCACCCCTTTTTTTTCCTGCCTCAATATCTTGATATGTTATGTTTACTCCCAATCTCCCATT</u> TCTCTGAGCCTAAAGGAGAAAAGTCCCACCAACTACCAGACCAGAACACGAGCCCCTCTGGGCAGCAGGATTCCTAAGT <u>CAAAGACCAGTTTGACCCAAACTGGCCTTTTAAAATAATCAGGAGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCC</u> 60 <u>CCACTGTCCCTTCCATCTTGGAATGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCCTCAGAGTGCATTTCCTGGAGAC</u> <u>GGCAGGCTTAGGTCTCACTGACAGCATGCCAGACACAACTGAATCGAAGCAGGCCTGAAGCCTAGGTCAGGGTTTCAGGA</u> <u>GGGAGTCAGGGGTGGGAGGAGAAGGAGGAGGAGGAGGCCAGACTGGCCTTTCTCCCCATACTTCACCCCAGC</u> <u>AGAGGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTCCTGTAGCAAGCCCAGCC</u> 65 <u>GGTAATCCTCCTAATGAACCCACAAGGTCAATTCACAACTGATATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAG</u> 

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The predicted amino acid sequence of FCTR2 protein corresponding to the foregoing nucleotide sequence is reported in Table 2B. FCTR2 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the mitochondrial matrix space (certainty=0.4718) and seems to have no N-terminal signal sequence. The predicted molecular weight is 90346.9 Daltons.

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#### Table 2B. FCTR2 Protein Sequence (SEQ ID NO:4).

MQCDVGDGRLFRLSLKRALSSCPDLFGLSSRNELLASCGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCK
LHRAACLLGKRITVIHSKDCFLKGDTCTMAGYARLKNVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLDADGNGHLSSSEL
AQHVLKKQDLDEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLTCAVHGDLRPPIIWKRN
GLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPR
ITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLSVGNMFYVF
SDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNVRNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPL
PAKLSYDKSHDQVWVLSWGDVHKSRPSLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETM
MPLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAARQLLVDSVTDSVLGPNGDVTGTPHTSPDGRFIVSAAADSPWLHVQE
ITVRGEIQTLYDLQINSGISDLAFQRSFTESNQYNIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLF
GQYLLTPARESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV

In a BLASTN search it was also found that nucleotides 784-5502 of FCTR2 nucleic acid had 4672 of 4719 bases (99%) identical to *Homo sapiens* mRNA for KIAA1061 protein, partial cds (GenBank Acc:AB028984) (Table 2C).

# Table 2C. BLASTN of FCTR2 against *Homo sapiens* mRNA for KIAA1061 protein (SEQ ID NO:46)

```
>GI|5689458|DBJ|AB028984.1|AB028984 HOMO SAPIENS MRNA FOR KIAA1061 PROTEIN, PARTIAL
25
    CDS
            LENGTH = 4719
     SCORE = 9075 BITS (4578), EXPECT = 0.0
     IDENTITIES = 4672/4719 (99%)
30
     STRAND = PLUS / PLUS
    QUERY: 784 AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 843
              AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 60
    SBJCT: 1
35
              AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGGAATCTCTGTTCAGGGACTTAGATGCAG 903
    QUERY: 844
              SBJCT: 61
              AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGGAATCTCTGTTCAGGGACTTAGATGCAG 120
40
    QUERY: 904
              ATGGCAATGGCCACCTCAGCAGCTCCGAACTGGCTCAGCATGTGCTGAAGAAGCAGGACC 963
              ATGGCAATGGCCACCTCAGCAGCTCCGAACTGGCTCAGCATGTGCTGAAGAAGCAGGACC 180
    SBJCT: 121
              TGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACA 1023
    QUERY: 964
45
              SBJCT: 181
              TGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACA 240
    QUERY: 1024 GTGACAGCTCCCTGACCCTCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCC 1083
              50
              GTGACAGCTCCCTGACCCTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCC 300
    SBJCT: 241
    QUERY: 1084 TCGCCCCGAGGACAGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 1143
              SBJCT: 301
              TCGCCCCGAGGACAGGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 360
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		QUERY:	1144	CCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAAACCGGCTCACCC 1203	,
	5	SBJCT:	361	CCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGCTCACCC 420	
		QUERY:	1204	TGAACTTCCTGGACTTGGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 1263	,
		SBJCT:		TGAACTTCCTGGACTTGGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 480	
	10	QUERY:	1264	CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 1323	j
		SBJCT:		CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 540	
	15	QUERY:	1324	TGTTCCAGACCCACGTCCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 1383	ļ
		SBJCT:		TGTTCCAGACCCACGTCCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 600	
		QUERY:	1384	GCCAGGCACAGGAGCCTGGAGTGGCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 1443	ļ
	20	SBJCT:		GCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 660	
		QUERY:	1444	TGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 1503	ţ
		SBJCT:		TGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 720	
	25	~		TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAG 1563	}
5 <b>.</b>		SBJCT:		TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAG 780	
A STATE	30	~		GGGCATACACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 1623	}
The state		SBJCT:		GGGCATACACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 840	
	35	~ .		TCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 1683	5
Į.		SBJCT:		TCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 900	,
# 15 m	40	SBJCT:		GCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATC	>
Think make				ACTGTGAGATCCAGAGGCACCTCAAACCCACGGAAAAGATTTTCATGAGCTATGAAGAAA 1803	3
		SBJCT:			
Hen, H H man, H H	45			TCTGTCCTCAAAGAGNNNNNNTGCAACCCAGCCCTGCCAGTGGGTATCTGCAGTCAATG 1863	
		QUERY:	1864	TCCGGAACCGGTACATCTATGTGGCCCAGCCAGCACTGAGCAGAGTCCTTGTGGTCGACA 192	3
	50	SBJCT:	1081		<b>o</b>
		QUERY:	1924	TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 198	3
	55	SBJCT:	1141	TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 120	O
		QUERY:	1984	ATGACAAGTCACATGACCAAGTGTGGGTCCTGAGCTGGGGGGACGTGCACAAGTCCCGAC 204	3
	60	SBJCT:	1201	ATGACAAGTCACATGACCAAGTGTGGGTCCTGAGCTGGGGGGGACGTGCACAAGTCCCGAC 126	O
	00	QUERY:	2044	CAAGTCTCCAGGTGATCACAGAAGCCAGCACCGGCCAGAGCCAGCACCTCATCCGCACAC 210	3
		SBJCT:	1261	CAAGTCTCCAGGTGATCACAGAAGCCAGCACCGGCCAGAGCCAGCACCTCATCCGCACAC 1320	0
	65	QUERY:	2104	CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAACCTCATCATCAACCACATCA 216	3
		SBJCT:	1321	CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACATCA 1380	0
	70	QUERY:	2164	GGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 2223	3

		SBUCI:	1381	GGIIIGGCIICAICIICAACAAGICIGAICCIGCAGICCACAAGGIGGACCIGGAAACAA	1440
	_	~		TGATGCCCCTCAAGACCATCGGCCTGCACCACCATGGCTGCCCCAGGCCATGGCAC	
	5	SBJCT:	1441	TGATGCCCCTCAAGACCATCGGCCTGCACCACCATGGCTGCCCCAGGCCATGGCAC	1500
		QUERY:	2284	ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCCTCTGCTG	2343
	10	SBJCT:	1501	ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCCTCTGCTG	1560
		QUERY:	2344	CCCGACAGCTGCTCGTTGACAGTGTCACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA	2403
		SBJCT:	1561	CCCGACAGCTGCTCGTTGACAGTGTCACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA	1620
	15	QUERY:	2404	CAGGCACCCCACACATCCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC	2463
		SBJCT:	1621	CAGGCACCCCACACATCCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC	1680
	20	QUERY:	2464	CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC	2523
	20	SBJCT:	1681	CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC	1740
		QUERY:	2524	AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT	2583
	25	SBJCT:	1741	AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT	1800
		QUERY:	2584	ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGCTCCTGGAGCTGTCCACGG	2643
10 10 10 10 10 10 10 10 10 10 10 10 10 1	30	SBJCT:	1801		1860
Ţij.	50	QUERY:	2644	GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGCAGGGCCAGCTCAGCCCTNNN	2703
10 11 11 11 11 11 11 11 11 11 11 11 11 1		SBJCT:	1861		1920
i i	35	QUERY:	2704	NNNTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG	2763
4"k 4"		SBJCT:	1921	GGGGTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG	1980
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	40	QUERY:	2764	CCCGAGAGTCACTGTTCCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCAG	2823
H with think is	10	SBJCT:	1981	CCCGAGAGTCACTGTTCCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCAG	2040
THE SHIPS		QUERY:	2824	GTATAAANNNNNNACCACAGTGGTGTGGGTGAGGTATGAAGGGCCCAGAGCAGAG	2883
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	45	SBJCT:	2041	GTATAAAGGGGGGACCACAGTGGTGGGTGGGTGAGGTATGAAGGGCCCAGAGCAGAG	2100
ŧ***		QUERY:	2884	CCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC	2943
	50	SBJCT:	2101	CCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC	2160
		QUERY:	2944	ATTTTTACAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG	3003
		SBJCT:	2161	ATTTTTACAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG	2220
	55	QUERY:	3004	CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT	3063
		SBJCT:	2221	CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT	2280
	60	QUERY:	3064	ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTTCTG	3123
	00	SBJCT:	2281	ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTTAAAGGGATCATTTCTG	2340
		QUERY:	3124	TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA	3183
	65	SBJCT:	2341	TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA	2400
		QUERY:	3184	AGCAGACACCTCTGTCAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC	3243
	70	SBJCT:	2401	AGCAGACACCTCTGTCAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC	2460
	70				

		QUERY:	3244	AGACTTTGCCCTGACGGAGTGGCCCGGAAGCAGAGCCCGACCAGGAGCAGGGGCCTCCCT	3303
	5	SBJCT:	2461	AGACTTTGCCCTGACGGAGTGGCCCGGAAGCAGAGCCGACCAGGAGCAGGGGCCTCCCT	2520
		QUERY:	3304	CCCGAACTGAAAGCCCATCCGTCCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT	3363
		SBJCT:	2521	CCCGAACTGAAAGCCCATCCGCCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT	2580
	10	QUERY:	3364	CTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG	3423
		SBJCT:	2581	CTTGCTTTTCCTTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG	2640
		QUERY:	3424	CATCTTGGGGGAAATCACTCACTTTATTTTGGAAATTTTTGATTNNNNNNNNT	3483
	15	SBJCT:	2641	CATCTTGGGGGATGGGAAATCACTCACTTTATTTTGGAAATTTTTGATTAAAAAAAA	2700
		QUERY:	3484	TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACTATATCCTTC	3543
	20	SBJCT:	2701	TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACTATATCCTTC	2760
		QUERY:	3544	CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCCACATCCCACAGCCAGAAAGAA	3603
		SBJCT:	2761	CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCCACATCCCACAGCCAGAAAGAA	2820
	25	QUERY:	3604	AATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCCTGCTTCTCCAAGAGCAG	3663
		SBJCT:	2821	AATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCCTGCTTCTCCAAGAGCAG	2880
4	30	QUERY:	3664	ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAAACCAGAACA	3723
State done		SBJCT:	2881	ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAAACCAGAACA	2940
Į.,		QUERY:	3724	AGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC	3783
Lab Sala Sala Sala Sala Sala Sala Sala Sa	35			AGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC	
TH.				CCAGATTCAGGGCAGACTGGGCTTGCCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC	
E TE	40			CCAGATTCAGGGCAGACTGGGCTTGCCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC	
				AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAAC	
	15			AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAAC	
Hand	45			AGATTTTGTTTTCCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCCATCCCCGCATCA	
				AGATTTTGTTTTCCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA  GCACTGCAGAGAGAACACATTTCGGCGAGGGTTTTCTTACCCACATTCCCCAATCAAT	
	50 55	2		GCACTGCAGAGAGAACACATTTCGGCGAGGGTTTTCTTACCCACATTCCCCAATCAAT	
				ACACACACTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT	
		~		ACACACACTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT  ACACACACTGCAGAACCCAGAACAGAA	
				GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCT	
	60			CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCCACATA	
		SBJCT:	3361		3420
	65	QUERY:	4204	TGAGTGGAACTTACATGTGTCCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTTGG	4263
		SBJCT:	3421		3480
	<b></b>	QUERY:	4264	AGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC	4323
	70			18	159
				<del>-</del> -	

		SBJCT:	3481	AGAGGIGGICICACCACAGACGICIIIGCIAAIIIIGGCCACCIICACCIACIGACAIGAC	2240
	5	-		CAGGATTTTCCTTTGCCATTAAGGAATGAACTCTTTCAAGGAGAGAAACCCTAGACTCT	
				CAGGATTTTCCTTTGCCATTAAGGAATGAACTCTTTCAAGGAGAGAAACCCTAGACTCT	
				GTGTCACTCTCAACACACACACCTCCTTTCACTCCTGCCTG	
	10			GTGTCACTCTCAACACACACACCTCCTTTCACTCCTGCCTG	
				CCCCCGCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA	
				CCCCCGCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA	
				AACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTTT	
				AACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTATTT  TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAG	
	20	-		TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAG	
				TTTCACAGTAGCTGGGATGCATGGATGACCCATCTCACCCCNNNNNNNNCCTGCCTCAA	
	25				
	23			TATCTTGATATGTTATGTTTACTCCCAATCTCCCATTTTTACCACTAAAATTCTCCAACT	
***		_			
Hall Series	30			TTCATAAACNNNNNNNGGAAAAATTTCCATTGTATCAGCCCCTGACAGAAAAAGGATCT	
THE REAL PROPERTY.		_		TTCATAAACTTTTTTTTGGAAAAATTTCCATTGTATCAGCCCCTGACAGAAAAAGGATCT	
ka i	35	QUERY:	4804	CTGAGCCTAAAGGAGGAAAAGTCCCACCAACTACCAGACCAGAACACGAGCCCCTCTGGG	4863
ALL ALL		SBJCT:	4021		4080
¥	40	QUERY:	4864	CAGCAGGATTCCTAAGTCAAAGACCAGTTTGACCCAAACTGGCCTTTTAAAATAATCAGG	4923
Marie Stands	40	SBJCT:	4081		4140
Bright Street		QUERY:	4924	AGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCCCCACTGTCCCTTCCATCTTGGAA	4983
201	45	SBJCT:	4141	AGTGACAGAGTCAACTTCTGCAGCACCTGCTCTCCCCCACTGTCCCTTCCATCTTGGAA	4200
in it		QUERY:	4984	TGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCCTCAGAGTGCATTTCCTGGAGACGGC	5043
	50	SBJCT:	4201	TGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCCTCAGAGTGCATTTCCTGGAGACGGC	4260
	30	QUERY:	5044	AGGCTTAGGTCTCACTGACAGCATGCCAGACACAACTGAATCGAAGCAGGCCTGAAGCCT	5103
		SBJCT:	4261	AGGCTTAGGTCTCACTGACAGCATGCCAGACACACTGAATCGAAGCAGGCCTGAAGCCT	4320
	55	QUERY:	5104	AGGTCAGGGTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT	5163
		SBJCT:	4321	AGGTCAGGGTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT	4380
	60	QUERY:	5164	GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGGAGTCAGGGGTGGGAGAA	5223
		SBJCT:	4381	GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGGGGTGGGAGGAGAA	4440
	65	QUERY:	5224	GGAGGAAGAGGAAGGCCAGACTGGCCTTTCTCCCATACTTCACCCCAGCAGA	5283
				GGAGGAAGAGGGGAAGGCCAGACTGCCCTTTCTCCCATACTTCACCCCAGCAGA	
	70			GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTC	
		SBJCT:	4501	GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTC	4560

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The FCTR2 amino acid sequence has 473 of 810 amino acid residues (58%) identical to, and 616 of 810 residues (76%) positive with, the 850 amino acid residue proteins from *Homo* sapiens KIAA1263 Protein fragment (ptnr: TREMBLNEW-ACC:BAA86577) (SEQ ID NO:47) (Table 2D).

# Table 2D. BLASTP of FCTR2 against *Homo sapiens* KIAA1263 Protein fragment (SEQ ID NO:47)

ptnr:TREMBLNEW-ACC:BAA86577 KIAA1263 PROTEIN - Homo sapiens (Human), 850 aa

```
20
            (fragment)
               Length = 850
            Score = 2573 (905.7 bits), Expect = 2.0e-267, P = 2.0e-267
            Identities = 473/810 (58%), Positives = 616/810 (76%)
25
                             LFRLSLKRALSSCPDLFGLSSRNELLASCGKKFCSRGSRCVLSRKTGEPECQCLEACRPS 69
           QUERY: 10
                                                         + |
                                                                   ++
                                                                               | ||
                              LMRLRHKEKNQESSRVKGFMIQDGPFGSCENKYCGLGRHCVTSRETGQAECACMDLCKRH 99
           SBJCT: 40
30
                              YVPVCGSDGRFYENHCKLHRAACLLGKRITVIHSKDCFLKGDTCTMAGYARLKNVLLALQ 129
           QUERY: 70
                               |+++||+||
           SBJCT: 100 YKPVCGSDGEFYENHCEVHRAACLKKQKITIVHNEDCFFKGDKCKTTEYSKMKNMLLDLQ 159
           QUERY: 130 TRLQPLQEGDSRQ-DPASQKRLLVESLFRDLDADGNGHLSSSELAQHVLKKQDLDEDLLG 188
35
                                                      SBJCT: 160 NOKYIMOENENPNGDDISRKKLLVDOMFKYFDADSNGLVDINELTQ-VIKQEELGKDLFD 218
           QUERY: 189 CSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLTCAVHGD 248
                                       40
           SBJCT: 219 CTLYVLLKYDDFNADKHLALEEFYRAFQVIQLSLPEDQKLSITAATVGQSAVLSCAIQGT 278
           QUERY: 249 LRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVL 308
                               SBJCT: 279 LRPPIIWKRNNIILNNLDLEDINDFGDDGSLYITKVTTTHVGNYTCYADGYEQVYQTHIF 338
45
           QUERY: 309 QVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANG 368
                               SBJCT: 339 QVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKPQLGWLKNGIDITPKLSKQLTLQANG 398
50
           QUERY: 369 SELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLSVGNMFY 428
                                SBJCT: 399 SEVHISNVRYEDTGAYTCIAKNEAGVDEDISSLFVEDSARKTLANILWREEGLGIGNMFY 458
           OUERY: 429 VFSDDGIIVIHPVDCEIORHLKPTEKIFMSYEEICPOREKNATOPCOWVSAVNVRNRYIY 488
55
                               | | + | | | | | | + | | | | | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
                                                                                      SBJCT: 459 VFYEDGIKVIQPIECEFQRHIKPSEKLLGFQDEVCPKAEGDEVQRCVWASAVNVKDKFIY 518
           QUERY: 489 VAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRPSLQVIT 548
                               60
           SBJCT: 519 VAQPTLDRVLIVDVQSQKVVQAVSTDPVPVKLHYDKSHDQVWVLSWGTLEKTSPTLQVIT 578
           OUERY: 549 EASTGOSOHLIRT----PFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETMM 603
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SBJCT: 579 LASGNVPHHTIHTQPVGKQFDRVDDFFIPTTTLIITHMRFGFILHKDEAALQKIDLETMS 638
    QUERY: 604 PLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAARQLLVDSVTDSVLGPNGDVTG 663
5
              SBJCT: 639 YIKTINLKDYKCVPQSLAYTHLGGYYFIGCKPDSTGAVSPQVMVDGVTDSVIGFNSDVTG 698
    QUERY: 664 TPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQYN 723
                             | | + | | | | ++ | |
10
    SBJCT: 699 TPYVSPDGHYLVSINDVKGLVRVQYITIRGEIQEAFDIYTNLHISDLAFQPSFTEAHQYN 758
    QUERY: 724 IYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPAR 783
             11
                                              + | ++ | | | | | | | | + | | ++
     SBJCT: 759 IYGSSSTQTDVLFVELSSGKVKMIKSLKEPLKAEEWPWNRKNRQIQDSGLFGQYLMTPSK 818
15
    QUERY: 784 ESLFLINGRQNTLRCEVSGIKGGTTVVWVGE 814
             +|||++||| | | ||++ ++ | ||+||+
     SBJCT: 819 DSLFILDGRLNKLNCEITEVEKGNTVIWVGD 849
          Amino acids 123-815 of FCTR2 also have 693 of 693 amino acid residues (100%)
20
    identical to the 693 amino acid residue protein fragment of KIAA1061 Protein from Homo
    sapiens (ptnr: TREMBLNEW-ACC: BAA83013) (SEQ ID NO:48) (Table 2E).
      Table 2E. BLASTP of FCTR2 against KIAA1061 Protein [Fragment] (SEQ ID NO:48)
25
          ptnr:TREMBLNEW-ACC:BAA83013 KIAA1061 PROTEIN - Homo sapiens (Human),
     693 aa (fragment).
             Length = 693
     Score = 3623 (1275.4 bits), Expect = 0.0, P = 0.0
30
     Identities = 693/693 (100%), Positives = 693/693 (100%)
     QUERY: 123 NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLDADGNGHLSSSELAQHVLKKQDL 182
              SBJCT: 1
             NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLDADGNGHLSSSELAQHVLKKQDL 60
35
     OUERY: 183 DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 242
              SBJCT: 61
             DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 120
40
     QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302
              SBJCT: 121 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEOL 180
     OUERY: 303 FOTHVLOVNVPPVIRVYPESOAOEPGVAASLRCHAEGIPMPRITWLKNGVDVSTOMSKQL 362
45
              SBJCT: 181 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 240
     QUERY: 363 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLS 422
              50
     SBJCT: 241 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLS 300
     QUERY: 423 VGNMFYVFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 482
              SBJCT: 301 VGNMFYVFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 360
55
     QUERY: 483 RNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 542
              SBJCT: 361 RNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 420
60
     QUERY: 543 SLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETM 602
```

SBJCT: 421 SLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETM 480

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QUERY: 603 MPLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAARQLLVDSVTDSVLGPNGDVT 662
            SBJCT: 481 MPLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAARQLLVDSVTDSVLGPNGDVT 540
5
    QUERY: 663 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 722
            SBJCT: 541 GTPHTSPDGRFIVSAAADSPWLHVOEITVRGEIOTLYDLOINSGISDLAFORSFTESNOY 600
10
    QUERY: 723 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 782
            SBJCT: 601 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 660
    QUERY: 783 RESLFLINGRONTLRCEVSGIKGGTTVVWVGEV 815
15
            SBJCT: 661 RESLFLINGRONTLRCEVSGIKGGTTVVWVGEV 693
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The amino acid sequence of the FCTR2 protein has 451 of 772 amino acid residues (58%) identical to, and 586 of 772 residues (75%) positive with, the 773 amino acid residue proteins hypothetical protein DKFZp566D234.1 from Homo sapiens (fragments) (ptnr: SPTREMBL-ACC: CAB70877.1) (SEQ ID NO:49) (Table 2F).

Table 2F. BLASTP of FCTR2 against hypothetical protein DKFZp566D234.1 (SEQ ID NO:49)

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Hall flads offers
  25
        >GI|11360192|PIR||T46283 HYPOTHETICAL PROTEIN DKFZP566D234.1 - HUMAN (FRAGMENTS)
        GI 6808053 EMB CAB70877.1 (AL137695) HYPOTHETICAL PROTEIN [HOMO SAPIENS]
                LENGTH = 773
ļķ
        SCORE = 911 BITS (2354), EXPECT = 0.0
Will Will
  30
        IDENTITIES = 451/772 (58%), POSITIVES = 586/772 (75%), GAPS = 7/772 (0%)
        OUERY: 49
                 CVLSRKTGEPECOCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKRITVIHSKDCFL 108
                 Hall mark that many
                 CVTSRETGOAECACMDLCKRHYKPVCGSDGEFYENHCEVHRAACLKKQKITIVHNEDCFF 61
        SBJCT: 2
  35
        QUERY: 109 KGDTCTMAGYARLKNVLLALQTRLQPLQEGDSRQ-DPASQKRLLVESLFRDLDADGNGHL 167
                                       + | | ++
                         +++||+||+
                                              | |+|+|||++|+ ||||
                 KGDKCKTTECSKMKNMLLDLONORYIMOENENPNGDDISRKKLLVDQMFKYFDADSNDLV 121
        SBJCT: 62
  40
        QUERY: 168 SSSELAQHVLKKQDLDEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDR 227
                                       + | | | + | + + + | + | | + |
        SBJCT: 122 DINELTQ-VIKQEELGKDLFDCTLYVLLKYDDFNADKHLALEEFYRAFQVIQLSLPEDQK 180
        QUERY: 228 XXXXXXXXXXXXXXXXXXXAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTI 287
  45
                              SBJCT: 181 LSITAATVGOSAVLSCAIOGTLRPPIIWKRNNIILNNLGLEDINDFGDDGSLYITKVTTT 240
        QUERY: 288 HMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW 347
                 50
        SBJCT: 241 HVGNYTCYADGYEQVYQTHIFQVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKPQLGW 300
        QUERY: 348 LKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSA 407
                 SBJCT: 301 LKNGIDITPKLSKOLTLQANGSEVHISNVRYEDTGAYTCIAKNEAGVDEDISSLFVEDSA 360
  55
        QUERY: 408 RKTLANILWREEGLSVGNMFYVFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQRE 467
                 SBJCT: 361 RKTLANILWREEGLGIGNMFYVFYEDGIKVIOPIECEFORHIKPSEKLLGFODEVCPIAE 420
  60
        QUERY: 468 KNATQPCQWVSAVNVRNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHD 527
                    SBJCT: 421 GDEVQRCVWASAVNVKDKFIYVAQPTLDRVLIVDVQSQKVVQAVSTDPVPVKLHYDKSHD 480
```

22

```
OUERY: 528 QVWVLSWGDVHKSRPSLQVITEASTGQSQHLIRT----PFAGVDDFFIPPTNLIINHIR 582
                | | | | | | | | | | | + |
                                          SBJCT: 481 QVWVLSWGTLEKTSPTLQVITLASGNVPHHTIHTQPVGKQFDRVDDFFIPTTTLIITHMR 540
     OUERY: 583 FGFIFNKSDPAVHKVDLETMMPLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAA 642
 5
                ||||| +| + |+ |+||||| +||| | + ||||++|+|||||+|| |+ ||
     SBJCT: 541 FGFILHKDEAALQKIDLETMSYIKTINLKDYKCVPQSLAYTHLGGYYFIGCKPDSTGAVS 600
     QUERY: 643 RQLLVDSVTDSVLGPNGDVTGTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQ 702
10
                 |++|| ||||+| | ||||++||
                                                     + || ||+|||| +|+
     SBJCT: 601 PQVMVDGVTDSVIGFNSDVTGTPYVSPDGHYLVSINDVKGLVRVQYITIRGEIQEAFDIY 660
     OUERY: 703 INSGISDLAFQRSFTESNQYNIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWG 762
                   15
     SBJCT: 661 TNLHISDLAFQPSFTEAHQYNIYGSSSTQTDVLFVELSSGKVKMIKSLKEPLKAEEWPWN 720
     OUERY: 763 GTHRIMRDSGLFGQYLLTPARESLFLINGRQNTLRCEVSGIKGGTTVVWVGE 814
                  SBJCT: 721 RKNRQIQDSGLFGQYLMTPSKDSLFILDGRLNKLNCEITEVEKGNTVIWVGD 772
20
            The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%)
     identical to, and 90 of 194 residues (45%) positive with, the 306 amino acid residue protein
     Follastin-Related Protein 1 Precursor from Rattus Norvegicus (ptnr: GenBank Acc:Q62632)
     (SEO ID NO:50) (Table 2G).
      Table 2G. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from Rattus
25
                                 Norvegicus (SEQ ID NO:50)
      >GI|2498392|SP|Q62632|FRP RAT FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR
       GI 1083669 PIR | S51361 FOLLISTATIN-RELATED PROTEIN PRECURSOR - RAT
      GI 536900 GB AAA66063.1 (U06864) FOLLISTATIN-RELATED PROTEIN PRECURSOR [RATTUS
30
      NORVEGICUS]
               LENGTH = 306
       SCORE = 86.4 BITS (213), EXPECT = 1E-15
       IDENTITIES = 61/194 (31%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)
35
      OUERY: 38 CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
                    CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 87
      SBJCT: 29
                ITVIHSKDCFLKGD-----TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
40
      QUERY: 98
                | | + | |
                                     |+ ++ |+ +|
               IQVDYDGHCKEKKSVSPSASPVVCYQANRDELRRRIIQWLEAEIIP----DGWFSKGSNY 143
      SBJCT: 88
      OUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLK------KQDLDEDLLGCSPGDLLRF 197
45
                  +++ |+ |+ |+ || || + |+
      SBJCT: 144 SEILDKYFKSFD-NGDSHLDSSEFLKFVEQNETAVNITAYPNQENNKLLRGLCVDALIEL 202
      OUERY: 198 DDYNSDSSLTLREF 211
                 | |+ | |+ + | |
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SBJCT: 203 SDENADWKLSFQEF 216

The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%) identical to, and 89 of 194 residues (45%) positive with, the 306 amino acid residue protein Follastin-Related Protein 1 Precursor from *Mus musculus* (GenBank Acc:Q62356) (SEQ ID NO:51) (Table 2H).

# Table 2H. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from Mus musculus (SEO ID NO:51)

```
>GI | 6679871 | REF | NP 032073.1 | FOLLISTATIN-LIKE [MUS MUSCULUS]
      GI 2498391 SP Q62356 FRP MOUSE FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR (TGF-BETA-
 5
      INDUCIBLE PROTEIN
                TSC-36)
      GI|481186|PIR||S38251 FOLLISTATIN-RELATED PROTEIN - MOUSE
      GI|349006|GB|AAC37633.1| (M91380) TGF-BETA-INDUCIBLE PROTEIN [MUS MUSCULUS]
               LENGTH = 306
10
      SCORE = 85.2 BITS (210), EXPECT = 3E-15
      IDENTITIES = 61/194 (31%), POSITIVES = 89/194 (45%), GAPS = 26/194 (13%)
     QUERY: 38 CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
15
                    CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 87
      SBJCT: 29
                ITVIHSKDCFLKGDT-----CTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
     QUERY: 98
                                      1 1
                                              |+ |+ |+ + |
                | | +
20
                IOVDYDGHCKEKKSASPSASPVVCYQANRDELRRRLIQWLEAEIIP----DGWFSKGSNY 143
      SBJCT: 88
      QUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLKK-----QDLDEDLLGCSPGDLLRF 197
                  +++ |+ |+ || || + |+
                                                         + ++
      SBJCT: 144 SEILDKYFKSFD-NGDSHLDSSEFLKFVEQNETAINITTYADQENNKLLRSLCVDALIEL 202
25
      OUERY: 198 DDYNSDSSLTLREF 211
                 | |+ | |+ + | |
      SBJCT: 203 SDENADWKLSFQEF 216
            The amino acid sequence of the FCTR2 protein has 63 of 193 amino acid residues (32%)
30
      identical to, and 89 of 193 residues (45%) positive with, the 299 amino acid residue protein
      Follastatin-Related Protein from the African Clawed Frog (GenBank Acc: JG0187) (SEQ ID
      NO:52) (Table 2I).
      Table 2I. BLASTP of FCTR2 against Follastatin-Related Protein from the African Clawed
35
                                     Frog (SEQ ID NO:52)
      >GI|7512162|PIR||JG0187 FOLLISTATIN-RELATED PROTEIN - AFRICAN CLAWED FROG
               LENGTH = 299
       SCORE = 81.8 BITS (201), EXPECT = 3E-14
40
       IDENTITIES = 63/193 (32%), POSITIVES = 89/193 (45%), GAPS = 25/193 (12%)
                CGKKFCSRGSRCVLSRKTGEPECOCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
                       | | ++ | |+| | +| |+
                                                 CANVFCGAGRECAVTEK-GDPTCDCIEKCKSHKRPVCGSNGKTYLNHCELHRDACLTGSK 86
      SBJCT: 28
45
                ITVIHSKDCFLK-GDT-----CTMAGYARL-KNVLLALQTRLQPLQEGDSRQDPASQK 148
      QUERY: 98
                       +
                                             ++ |+ || + |
                IQVDYDGHCKEKTSDTPAAVPVACYQSDRDEMRRRVIHWLQTEITP----DGWFSKGSDY 142
      SBJCT: 87
50
      QUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLKKQDL-----DED----LLGCSPGDLLRFD 198
                  +++ |+ | | |+ | |+ | |+ |
                                                       +
      SBJCT: 143 SEILDRYFKKFD-DGDSHLDSAELQSFLEQSQSTNITTYKDEETNRMLKSLCVEALIELS 201
      QUERY: 199 DYNSDSSLTLREF 211
55
                 | |+| |
      SBJCT: 202 DENADWKLNKNEF 214
```

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The amino acid sequence of the FCTR2 protein has 59 of 194 amino acid residues (30%) identical to, and 90 of 194 residues (45%) positive with, the 308 amino acid residue protein Follistatin-Related Protein 1 Precursor from *Homo sapiens* (GenBank Acc:Q12841) (SEQ ID NO:53) (Table 2J).

# Table 2J. BLASTP of FCTR2 against Follistatin-Related Protein 1 Precursor from *Homo*sapiens (SEQ ID NO:53)

```
>GI|5901956|REF|NP 009016.1| FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
      GI 2498390 SP 012841 FRP HUMAN FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR
      GI 1082372 PIR | S51362 FOLLISTATIN-RELATED PROTEIN - HUMAN
10
      GI|536898|GB|AAA66062.1| (U06863) FOLLISTATIN-RELATED PROTEIN PRECURSOR [HOMO
      SAPIENS]
      GI 3184393 DBJ BAA28707.1 (D89937) FOLLISTATIN-RELATED PROTEIN (FRP) [HOMO SAPIENS]
      GI 12652619 GB AAH00055.1 AAH00055 (BC000055) FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
               LENGTH = 308
15
       SCORE = 82.9 BITS (204), EXPECT = 1E-14
       IDENTITIES = 59/194 (30%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)
      QUERY: 38 CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
20
                       | | ++ | | | | | + | + |
                                                  CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 89
      SBJCT: 31
      QUERY: 98
                ITVIHSKDCFLKGD-----TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
                                      1 +
                                              |+ ++ |+ +|
25
                IQVDYDGHCKEKKSVSPSASPVVCYQSNRDELRRRIIQWLEAEIIP----DGWFSKGSNY 145
      SBJCT: 90
      QUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLKK------QDLDEDLLGCSPGDLLRF 197
                       |++ | +|+ | ||| + | +
                                                          + ++ | |
      SBJCT: 146 SEILDKYFKNFD-NGDSRLDSSEFLKFVEQNETAINITTYPDQENNKLLRGLCVDALIEL 204
30
      QUERY: 198 DDYNSDSSLTLREF 211
                  | |+|
                       |+ +||
      SBJCT: 205 SDENADWKLSFQEF 218
```

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The amino acid sequence of the FCTR2 protein has 35 of 69 amino acid residues (50%) identical to, and 45 of 69 residues (64%) positive with, the 315 amino acid residue Flik protein [Gallus gallus] (EMBL Acc:CAB42968.1) (SEQ ID NO:54) (Table 2K).

### Table 2K. BLASTP of FCTR2 against Flik protein [Gallus gallus] (SEQ ID NO:54)

```
>GI | 4837645 | EMB | CAB42968.1 | (AJ238977) FLIK PROTEIN [GALLUS GALLUS]
40
              LENGTH = 315
      SCORE = 79.8 BITS (196), EXPECT = 1E-13
      IDENTITIES = 35/69 (50%), POSITIVES = 45/69 (64%), GAPS = 1/69 (1%)
45
     QUERY: 38
              CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
                   SBJCT: 31
               CANVFCGRGAECAVTEK-GEPTCLCIEQCKPHGRPVCGSNGKTYLNHCELHRDACLTGSK 89
     QUERY: 98
               ITVIHSKDC 106
50
               +
     SBJCT: 90 IQVDYDGHC 98
```

The amino acid sequence of the FCTR2 protein has 49 of 152 amino acid residues (32%) identical to, and 65 of 152 residues (42%) positive with a 272-420 amino acid fragment and, 31

50

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of 83 residues (37%) identical to and 44 of 83 residues (52%) positive with a 248-329 amino acid fragment, both of the 1375 amino acid residue Frazzled gene protein [*Drosophila melanogaster*] (GenBankAcc:T13822) (SEQ ID NO:55) (Table 2L).

# Table 2L. BLASTP of FCTR2 against Frazzled gene protein [Drosophila melanogaster] (SEO ID NO:55)

```
>GI|7511861|PIR||T13822 FRAZZLED GENE PROTEIN - FRUIT FLY (DROSOPHILA MELANOGASTER)
       GI 1621115 GB AAC47314.1 (U71001) FRAZZLED [DROSOPHILA MELANOGASTER]
               LENGTH = 1375
10
       SCORE = 69.4 BITS (169), EXPECT = 2E-10
       IDENTITIES = 49/152 (32%), POSITIVES = 65/152 (42%), GAPS = 4/152 (2%)
      QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301
                   + | + | | | | | | + | + | | | + |
                                                   15
      SBJCT: 272 CVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGSLQISSAEDIDSGNYQCRASNTVDS 331
      QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQ 361
                                               |+|
                                                   | | | | | | | | ++
      SBJCT: 332 LDAQATVQVQEPPKFIKAPKDTTAHEKDEPELKCDIWGKPKPVIRWLKNGDLITPNDYMQ 391
20
      OUERY: 362 LSLLANGSELHISSVRYEDTGAYTCIAKNEVG 393
                    | + | | | + | | + | + |
      SBJCT: 392 --- LVDGHNLKILGLLNSDAGMFQCVGTNAAG 420
25
      SCORE = 52.9 BITS (126), EXPECT = 1E-05
       IDENTITIES = 31/83 (37%), POSITIVES = 44/83 (52%), GAPS = 2/83 (2%)
      QUERY: 311 NVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVS-TQMSKQLSLLANGS 369
                                     30
      SBJCT: 248 SVAPSFLVGPSPKTVREGDTVTLDCVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGS 307
      QUERY: 370 ELHISSVRYEDTGAYTCIAKNEV 392
                          |+| | | | |
                  SBJCT: 308 -LQISSAEDIDSGNYQCRASNTV 329
35
```

The amino acid sequence of the FCTR2 protein has 53 of 177 amino acid residues (29%) identical to, and 78 of 177 residues (43%) positive with a 366-539 amino acid fragment, 51 of 170 residues (30%) identical to and 74 of 170 residues (43%) positive with a 276-438 amino acid fragment, 46 of 165 amino acid residues (27%) identical to, and 74 of 165 amino acid residues positive with a 185-341 amino acid fragment, 48 of 167 amino acid residues (28%) identical to and 70 of 167 amino acid residues (41%) positive with a 77-243 amino acid fragment, and 28 of 84 amino acid residues (33%) and 37 of 84 amino acid residues positive with a 56-139 amino acid fragment all of the protein 1395 residue Roundabout 1 protein [*Drosophila melanogaster*] (GenBankAcc:AAC38849.1) (SEQ ID NO:56) (Table 2M).

# Table 2M. BLASTP of FCTR2 against Roundabout 1 protein [Drosophila melanogaster] (SEQ ID NO:56)

```
>GI | 2804782 | GB | AAC38849.1 | (AF040989) ROUNDABOUT 1 [DROSOPHILA MELANOGASTER]

LENGTH = 1395

SCORE = 69.8 BITS (170), EXPECT = 1E-10

IDENTITIES = 53/177 (29%), POSITIVES = 78/177 (43%), GAPS = 11/177 (6%)
```

```
QUERY: 243 CAVHGDLRPPIIWKRNGL-TLNFLDLEDINDF-GEDDSLYITKVTTIHMGNYTCHA---- 296
                SBJCT: 366 CMASGNPPPSVFWTKEGVSTLMFPNSSHGRQYVAADGTLQITDVRQEDEGYYVCSAFSVV 425
   5
       QUERY: 297 --SGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDV 354
                 SBJCT: 426 DSSTVRVFLQVSSVDERPPPIIQIGPANQTLPKGSVATLPCRATGNPSPRIKWFHDGHAV 485
       QUERY: 355 STQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTL 411
  10
                 | + |++ || | + ++ |+| || | | ++| +|
       SBJCT: 486 --QAGNRYSII-QGSSLRVDDLQLSDSGTYTCTASGERGETSWAATLTVEKPGSTSL 539
       SCORE = 56.3 BITS (135), EXPECT = 1E-06
  15
        IDENTITIES = 51/170 (30%), POSITIVES = 74/170 (43%), GAPS = 12/170 (7%)
       OUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301
                 |+||| ++||+ + ++| + || |+ +| | | | + |
       SBJCT: 276 CSVGGDPPPKVLWKKEEGNIPVSRARILHD---EKSLEISNITPTDEGTYVCEAHNNVGO 332
  20
       QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM--- 358
       QUERY: 359 -SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSA 407
  25
                     +| | + | | | | + | |
       SBJCT: 391 SSHGRQYVAADGTLQITDVRQEDEGYYVCSAFSV--VDSSTVRVFLQVSS 438
       SCORE = 51.7 BITS (123), EXPECT = 3E-05
  30
        IDENTITIES = 46/165 (27%), POSITIVES = 74/165 (43%), GAPS = 20/165 (12%)
       QUERY: 251 PPIIWKRNGLTLNFLDLEDINDFG------EDDSLYITKVTTIHMGNYTCHASG---- 298
                 SBJCT: 185 PTLIWIKDGVPLD--DLKAMS-FGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGT 241
ani:
  35
       QUERY: 299 HEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM 358
                 | + ++|| | |+ | |+ | |++ | ++
       SBJCT: 242 RESSYAKLIVQVK--PYFMKEPKDQVMLYGQTATFHCSVGGDPPPKVLWKKEEGNIPVSR 299
       QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFI 403
  40
                 ++ + + + | | | ++ | | | | | | | | | |
       SBJCT: 300 AR---ILHDEKSLEISNITPTDEGTYVCEAHNNVGQISARASLIV 341
       SCORE = 44.0 BITS (103), EXPECT = 0.007
        IDENTITIES = 48/167 (28%), POSITIVES = 70/167 (41%), GAPS = 13/167 (7%)
  45
       QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHM----GNYTCHASG 298
                 SBJCT: 77 CKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFFYRTMQGKKEQDGGEYWCVAKN 136
  50
        OUERY: 299 H-EQLFQTHV-LQVNV-PPVIRVYPESQAQEPGVAASLRCH-AEGIPMPRITWLKNGVDV 354
                   SBJCT: 137 RVGQAVSRHASLQIAVLRDDFRVEPKDTRVAKGETALLECGPPKGIPEPTLIWIKDGVPL 196
  55
        OUERY: 355 STOMSKQLSL----LANGSELHISSVRYEDTGAYTCIAKNEVGVDE 396
                        SBJCT: 197 DDLKAMSFGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGTRE 243
        SCORE = 42.9 BITS (100), EXPECT = 0.014
  60
        IDENTITIES = 28/84 (33%), POSITIVES = 37/84 (43%), GAPS = 4/84 (4%)
        OUERY: 314 PVIRVYPESOAOEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELH- 372
                 SBJCT: 56 PRIIEHPTDLVVKKNEPATLNCKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFF 115
  65
        QUERY: 373 ---ISSVRYEDTGAYTCIAKNEVG 393
                   + + + | | | + | | |
        SBJCT: 116 YRTMQGKKEQDGGEYWCVAKNRVG 139
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The amino acid sequence of the FCTR2 protein has 55 of 157 amino acid residues (35%) identical to, and 75 of 157 residues (47%) positive with a 620-775 amino acid fragment, 49 of 163 residues (30%) identical to and 71 of 163 residues (43%) positive with a 335-492 amino acid fragment, 32 of 85 amino acid residues (37%) identical to, and 48 of 85 amino acid residues (55%) positive with a 1305-1388 amino acid fragment, 37 of 143 amino acid residues (25%) identical to and 60 of 143 amino acid residues (41%) positive with a 183-319 amino acid fragment, 43 of 174 amino acid residues (24%) and 70 of 174 amino acid residues (39%) positive with a 711-884 amino acid fragment, and 46 of 165 residues (27%) identical to and 69 of 165 residues positive with a 831-884 amino acid fragment all of the protein 1395 residue Down Syndrome Cell Adhesion Molecule Precursor (CHD2) from Homo Sapiens (GenBankAcc:O60469) (SEQ ID NO:57) (Table 2N).

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### Table 2N. BLASTP of FCTR2 against Down Syndrome Cell Adhesion Molecule Precursor (SEO ID NO:57)

```
15
        >gi|12643619|sp|060469|DSCA HUMAN DOWN SYNDROME CELL ADHESION MOLECULE PRECURSOR
         (CHD2)
         GI 6740013 GB AAF27525.1 AF217525 1 (AF217525) DOWN SYNDROME CELL ADHESION MOLECULE
         [HOMO SAPIENS]
                 LENGTH = 2012
### ### 1
# # # # #
  20
         SCORE = 70.6 BITS (172), EXPECT = 6E-11
         IDENTITIES = 55/157 (35%), POSITIVES = 75/157 (47%), GAPS = 7/157 (4%)
        QUERY: 245 VHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQ 304
  25
                          | |+++| +
                                          ++
                                                 SBJCT: 620 VSGDLPITITWQKDGRPIPGSLGVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAAVE 679
        QUERY: 305 THV-LQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-LKNGVDVST----QM 358
                      30
        SBJCT: 680 HQSQLIVRVPPKFVVQPRDQDGIYGKAVILNCSAEGYPVPTIVWKFSKGAGVPQFQPIAL 739
        QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVD 395
                  SBJCT: 740 NGRIQVLSNGS-LLIKHVVEEDSGYYLCKVSNDVGAD 775
  35
        SCORE = 50.6 BITS (120), EXPECT = 7E-05
         IDENTITIES = 49/163 (30%), POSITIVES = 71/163 (43%), GAPS = 16/163 (9%)
        QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302
  40
                                                 ++ | + +
                   |+|
                            + | | | | | |
        SBJCT: 335 CSVTGTEDQELSWYRNGEILNPGKNVRITGINHEN-LIMDHMVKSDGGAYQCFVRKDKLS 393
        QUERY: 303 FQTH---VLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW----
                        | | +
                              | + | + | +
                                          45
        SBJCT: 394 AQDYVQVVLEDGTPKIISAFSE-KVVSPAEPVSLMCNVKGTPLPTITWTLDDDPILKGG- 451
        QUERY: 353 DVSTQMSKQLSLLAN-GSELHISSVRYEDTGAYTCIAKNEVGV 394
                    ++ + ++
                               SBJCT: 452 -- SHRISQMITSEGNVVSYLNISSSQVRDGGVYRCTANNSAGV 492
  50
        SCORE = 47.9 BITS (113), EXPECT = 5E-04
         IDENTITIES = 32/85 (37%), POSITIVES = 48/85 (55%), GAPS = 6/85 (7%)
        QUERY: 333 LRCHAEGIPMPRITWLK--NGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKN 390
  55
                    + + |+ +||| + | +|+ ||+| |+|||
        SBJCT: 1305 LPCKAVGDPSPAVKWMKDSNGTPSLVTIDGRRSIFSNGSFI-IRTVKAEDSGYYSCIANN 1363
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QUERY: 391 EVGVDEDISSLFIE---DSARKTLA 412
                      | | | | + | ++ | | | | ++
        SBJCT: 1364 NWGSDEIILNLQVQVPPDQPRLTVS 1388
   5
        SCORE = 42.9 BITS (100), EXPECT = 0.015
         IDENTITIES = 37/143 (25%), POSITIVES = 60/143 (41%), GAPS = 6/143 (4%)
        QUERY: 270 INDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGV 329
                   | | + | | | + | |
                                      | +|| +
                                                       10
        SBJCT: 183 IKDVQNEDGLYNYRCITRHRYTGETRQSNSARLFVSD--PANSAPSILDGFDHRKAMAGQ 240
        QUERY: 330 AASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAK 389
                     SBJCT: 241 RVELPCKALGHPEPDYRWLKD--NMPLELSGRFQKTVTG--LLIENIRPSDSGSYVCEVS 296
  15
        QUERY: 390 NEVGVDEDISSLFIEDSARKTLA 412
                     + |
                            +++
                                   + |++
        SBJCT: 297 NRYGTAKVIGRLYVKQPLKATIS 319
  20
         SCORE = 41.3 BITS (96), EXPECT = 0.047
         IDENTITIES = 43/174 (24%), POSITIVES = 70/174 (39%), GAPS = 11/174 (6%)
        OUERY: 243 CAVHGDLRPPIIWK--RNGLTLNF--LDLEDINDFGEDDSLYITKVTTIHMGNYTCHASG 298
                   |+ | | + | + |
                                                     + | | |
  25
        SBJCT: 711 CSAEGYPVPTIVWKFSKGAGVPQFQPIALNGRIQVLSNGSLLIKHVVEEDSGYYLCKVSN 770
        OUERY: 299 H -- EQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVST 356
                       + ++ | | + | | +
                                                   + | |
        SBJCT: 771 DVGADVSKSMYLTVKIPAMITSYPNTTLATQGQKKEMSCTAHGEKPIIVRWEKEDRIINP 830
JJ 30
        QUERY: 357 QMSKQLSLLANGSELHISSVRY-----EDTGAYTCIAKNEVGVDEDISSLFIED 405
£ij.
                              | | | +++
                                         SBJCT: 831 EMARYLVSTKEVGEEVISTLQILPTVREDSGFFSCHAINSYGEDRGIIQLTVQE 884
1 35
        SCORE = 40.6 BITS (94), EXPECT = 0.074
         IDENTITIES = 46/165 (27%), POSITIVES = 69/165 (40%), GAPS = 7/165 (4%)
TH.
        QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTT-IHMGNYTCHASGHEQ 301
                            | + |
                                    | + + | ++ | + | | | | +
  40
        SBJCT: 525 CRVIGYPYYSIKWYKNSNLLPFNHRQVA--FENNGTLKLSDVQKEVDEGEYTCNVLVQPQ 582
        QUERY: 302 LFQTHVLQVN--VPPVIRVYPESQAQEPGVAASLRCHAEGIPMP-RITWLKNGVDVSTQM 358
                     + + | | | | | + + |
                                            + |
                                                          +| || |+|
        SBJCT: 583 LSTSQSVHVTVKVPPFIQPF-EFPRFSIGQRVFIPCVVVSGDLPITITWQKDGRPIPGSL 641
  45
        QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFI 403
                            | | | ++
                                        | | | | | | + | |
                                                     | | +
        SBJCT: 642 GVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAAVEHQSQLIV 686
```

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Homo sapiens* (SWISSPROT Acc:Q13449) (SEQ ID NO:58) (Table 20).

## Table 20. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (SEQ ID NO:58)

PTNR:SWISSPROT-ACC:Q13449 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR (LSAMP) - HOMO SAPIENS (HUMAN), 338 AA.

LENGTH = 33860 SCORE = 191 (67.2 BITS), EXPECT = 6.7E-12, P = 6.7E-12IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)

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The amino acid sequence of the FCTR2 protein has 68 of 190 amino acid residues (35%) identical to, and 92 of 190 residues (48%) positive with Putative Neuronal Cell Adhesion Molecule, Short Form from Mus musculus (SPTREMBL Acc: O70246) (SEQ ID NO:59) (Table 2P).

## Table 2P. BLASTP of FCTR2 against Putative Neuronal Cell Adhesion Molecule, Short Form from Mus musculus (SEQ ID NO:59)

```
PTNR:SPTREMBL-ACC:070246 PUTATIVE NEURONAL CELL ADHESION MOLECULE (PUNC)
      (PUTATIVE NEURONAL CELL ADHESION MOLECULE, SHORT FORM) - MUS MUSCULUS
10
      (MOUSE), 793 AA
                LENGTH = 793
       SCORE = 203 (71.5 BITS), EXPECT = 7.0E-12, SUM P(2) = 7.0E-12
       IDENTITIES = 68/190 (35%), POSITIVES = 92/190 (48%)
```

The amino acid sequence of the FCTR2 protein has 58 of 199 amino acid residues (29%) identical to, and 91 of 199 residues (45%) positive with CHLAMP, G11-Isoform Precursor from Gallus gallus (SPTREMBL Acc: O02869) (SEQ ID NO:60) (Table 2Q).

## Table 2Q. BLASTP of FCTR2 against CHLAMP, G11-Isoform Precursor from Gallus gallus (SEQ ID NO:60)

```
PTNR:SPTREMBL-ACC:002869 CHLAMP, G11-ISOFORM PRECURSOR - GALLUS GALLUS
(CHICKEN), 350 AA.
          LENGTH = 350
SCORE = 191 (67.2 BITS), EXPECT = 7.7E-12, P = 7.7E-12
IDENTITIES = 58/199 (29%), POSITIVES = 91/199 (45%)
```

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from Rattus norvegicus (SWISSPROT Acc:Q62813) (SEQ ID NO:61) (Table 2R).

## Table 2R. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SEQ ID NO:61)

```
PTNR:SWISSPROT-ACC:Q62813 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR
35
      (LSAMP) - RATTUS NORVEGICUS (RAT), 338 AA.
                LENGTH = 338
       SCORE = 188 (66.2 BITS), EXPECT = 1.5E-11, P = 1.5E-11
       IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)
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```

FCTR2 protein has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and

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reproductive physiology. Frazzled encodes a Drosophila member of the DCC immunoglobulin subfamily and is required for CNS and motor axon guidance (Cell 87:197-204(1996)). Characterization of a rat C6 glioma-secreted follistatin-related protein (FRP) and cloning and sequence of the human homologue is described in Eur. J. Biochem. 225:937-946(1994). This protein may modulate the action of some growth factors on cell proliferation and differentiation. FRP binds heparin. The follistatin-related protein is a secreted protein and has one follistatin-like domain. The cloning and early dorsal axial expression of Flik, a chick follistatin-related gene and evidence for involvement in dorsalization/neural induction is presented in Dev. Biol. 178:327-342(1996). Roundabout controls axon crossing of the CNS midline and defines a novel subfamily of evolutionarily conserved guidance receptors, as shown in Cell 92:205-215(1998). cDNA cloning and structural analysis of the human limbic-system- associated membrane protein (LAMP) is described in Gene 170:189-195(1996). LAMP, a protein of the OBCAM family that contains three immunoglobulin-like C2-type domains, mediates selective neuronal growth and axon targeting. LAMP contributes to the guidance of developing axons and remodeling of mature circuits in the limbic system. This protein is essential for normal growth of the hippocampal mossy fiber projection. LAMP is attached to the membrane by a GPI-Anchor. It is expressed on limbic neurons and fiber tracts as well as in single layers of the superior colliculus, spinal chord and cerbellum. Characterization of the human full-length PTK7 cDNA encoding a receptor protein tyrosine kinase-like molecule closely related to chick KLG is disclosed in J. Biochem. 119:235-239(1996). Based upon homology, FCTR2 proteins and each homologous protein or peptide may share at least some activity.

#### Functions and therapeutic uses:

The OMIM gene map has identified this region which the invention maps to (5q21-5q31) as associated with susceptibility to the following diseases (OMIM Ids are underlined):

- Allergy and asthma
  - Hemangioma,
  - capillary infantile Schistosoma mansoni infection, susceptibility/resistance to Spinocerebellar ataxia
  - Bronchial asthma
  - Plasmodium falciparum parasitemia,
  - intensity of Corneal dystrophy, Groenouw type I, <u>121900</u>; Corneal dystrophy,lattice type I, <u>122200</u>;
  - Reis-Bucklers corneal dystrophy; Corneal dystrophy, Avellino type Eosinophilia, familial Myelodysplastic syndrome;

- Myelogenous leukemia, Acute Cutis laxa, recessive, type I, Deafness, autosomal dominant nonsyndromic sensorineural, 1 Contractural arachnodactyly, Congenital Neonatal alloimmune thrombocytopenia;
- Glycoprotein Ia deficiency Male infertility;
- Charcot-Marie-Tooth neuropathy, Demyelinating Gardner syndrome;
  - Adenomatous polyposis coli;
  - Colorectal cancer;
  - Desmoid disease, hereditary, <u>135290</u>;
  - Turcot syndrome, 276300;
- Adenomatous polyposis coli, attenuated
  - Colorectal cancer

Therefore the invention is implicated in at least all of the above mentioned diseases and may have therapeutic uses for these diseases.

This sequence has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and reproductive physiology. Therefore the invention is also implicated in disorders such as or therapeutic uses for:

- Neurodegenerative disorders, nerve trauma, epilepsy, mental health conditions
- Tissue regeneration in vivo and in vitro

Female reproductive system disorders and pregnancy

#### FCTR3

FCTR3, is an amino acid type II membrane, neurestin-like protein. The FCTR3a nucleic acid of 1430 nucleotides (also designated 10129612.0.118) is shown in Table 3A. An ORF was identified beginning with an ATG initiation codon at nucleotides 69-71 and ending with a TAG codon at nucleotides 1212-1214. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3A, and the start and stop codons are in bold letters.

#### Table 3A. FCTR3a Nucleotide Sequence (SEQ ID NO:5)

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The FCTR3 polypeptide (SEQ ID NO:5) encoded by SEQ ID NO:5 is 381 amino acid residues and is presented using the one-letter code in Table 3B.

#### Table 3B. Encoded FCTR3a protein sequence (SEQ ID NO:6).

MLHAANKGRKPSAEAGRPIPPTSSPSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGP PNHHSQSTLRPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGS TPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIVPWSLKNSSIDSGEAEVG RRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFV QYLDVGLWHLAFYNDGKDKEMVSFNTVVLDGTI

In an alternative embodiment, the 5' end of the FCTR3a nucleic acid could be extended as it is in the 9826bp FCTR3b (also referred to herein as 10129612.0.405) shown in Table 3C. An ORF was identified beginning with an ATG initiation codon at nucleotides 280-282 and ending with a TAA codon at nucleotides 8479-8481. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3C, and the start and stop codons are in bold letters. Italicized bases 1-201 refer to a variable 5' region that will be further discussed below.

#### Table 3C. FCTR3b Nucleotide Sequence (SEQ ID NO:7)

TTTAAATCCTCATACCTTAAAGGAGATGTGTATATAAGGGAGTTGGAACCAGCATTAGATGAGTTGACAAAAATGCAGTT30 <u>AGTTGGCTGCTTTCCTGCTGAGACTTCTCATGGCAGAGACTGAGGGTGGCAAAGTGACAAGTGCCAAAACTCAGGCCTGA</u> ACGCTGTGGCAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACAGAAATCCTACA GCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACCGG 35 GAGTCAGATGAGTTTCCTAGACAAGGAACCAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAG GAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTCGT GAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTAC ATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGC 40 TAGACAGCAACACCTCCCATCAAATCATGGACACCCAACCCTGATGAGGAATTCTCCCCCCAATTCATACCTGCTCAGAGCA  $\tt CCCTCACAACCACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTC$ AGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACCACAGAGTCCGTTCAGCTTCAGGACAGCTGGGTGCTA AACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCAGCAGCTCTTC 45  $\tt CTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTGCCGCGCCCTCCTCTTG$ GCTATTTTGCTGGCGTATTTCATAGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCG ACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCATGCCCAGTATGACTTC 50 ATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCA GAATGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGAAAAGACAAAGAGA TGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGAATGTGTCC GGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAGCTGCCCTGTCCTGTGCAGTGGGAATGG ACAATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCCCATGAATCAGTGCATCG 55 

TGCATCGGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCAGCGTGTGACCACCCCCCCGCTGCAT 5 TGAGCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAA CGGCAGGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGGCAG TGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCCTGTGCTGATAACAAGGATAATGA 10 TTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCA AGTAGTAACTACAGATGGAACTCCCCTGGTCGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCA AGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTGGTGATGAAGACCGAGGAGAACTC CATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTG 15 CTTCGCTATCTGAGCTCTAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAA GAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAA 20 AGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCCGGAGCATTTCCTGTCCCAGCTGC AACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGA CTTCAATTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATA 25 GTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTG CAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCCACC GTGGCCAACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCG 30 GCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGA GAAGAAGATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACT GCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCCCCATCATCC TTAGCTGTAGCTCCAGATGGTACCATTTACATTGCAGACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCC 35 TGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCC ACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTCACATATAGTACTGACAATGATGTCACTGAATTG ATTGACAATAATGGGAATTCCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCA ATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAAGGC 40 CGCCTGACCAACGTGACGCGCCCCACGGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACAT TGAGAACTCCAACCGTGATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTACAAG ATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGCTTC CACAGCGAGCCCCATGTCCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGG 45 ATGGAAGAATCTCTTGTCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTCACC TGTCCCGCATGTTCGCTGACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAA CGTCAGTATATATTTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTCACCATGCCCAGCGTGGCCCGGCACAGCATGTC 50 CACACACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTG ATGACGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAGTTA  ${\tt TCAGAGATTGTCTACGACAGTACCGCCGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCACTCA$ AAGTGGGGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGG AAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATAAGT 55 GAGACTCCCCTCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCAT CTATTATGACATCAACCAGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGG GAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGC CGTCAATGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGC 60 GCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGATGGC TATCTGTGCCAGAGGGGTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGG GTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCCTACAAGACCAACCTGGGCCACCACCTGCAGTACT TCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTACTAC GACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCC 65 ACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGACCCCCTGACCAAGCTGGTCCACTTCACTCAGCGT GATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTT TAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCT GGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCTCCC 70 

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GGCCTTCATGGCTCTGGAAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTG

The FCTR3b polypeptide (SEQ ID NO:8) encoded by SEQ ID NO:7 is 2733 amino acid residues and is presented using the one-letter code in Table 3D. The protein has a predicted molecular weight of 303424.3 daltons.

## Table 3D. Encoded FCTR3b protein sequence (SEQ ID NO:8). MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNRVTDLIHRESDEFPRQGTNFTLAELGI

 ${\tt CEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDENGRPIP$ PTSSPSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNH  $\verb|TLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTV|$ YTPPPRLLPRNTFSRKAFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQI  ${\tt HISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDG}$ KDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDP SCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNW MGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHCTIGRQTAGTETDGCPDLCN GNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLD1IQQGQTDWPAVKS FYDRIKLLAGKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPF  ${\tt MSQERTVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLS}$ SRTAGYKSLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLILW EKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAV GIDGSLYVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAG  $\tt TGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPL$ TDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINRLRQ VTTNGEICLLAGAASDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPG  $\verb"EQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNL"$ ELGLMTYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASYTVVQ DOVRNSYOLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLL SIDYDRNIRTEKIYDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWS YSYLDKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVF YKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKP VISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELK  ${\tt LGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNPGNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDI$ FEYNSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAMESSSGE EYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVG KEPAPFNLYMFKSNNPLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQ AFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYF VKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTA WAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR

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In further alternative embodiments the italicized bases in the 5' end of the FCTR3b sequence in table 3C is a variable region. This region can be substituted for in other embodiments of FCTR3. The nucleotide sequence for 9823bp FCTR3c (also referred to herein as 10129612.0.154) has the same nucleotide sequence as FCTR3b except that the italicized region is replaced with the 201 base sequence shown in Table 3E. An ORF for the total FCTR3c nucleotide sequence was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3c. This open reading frame will translate the same amino acid sequence as shown in Table 3C for FCTR3b.

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#### Table 3E. Encoded FCTR3c 5'end nucleotide sequence (SEQ ID NO:9).

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In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3F to form 9823bp FCTR3d (also referred to herein as 10129612.0.67). An ORF was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3d. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

### Table 3F. Encoded FCTR3d 5'end nucleotide sequence (SEQ ID NO:10).

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3G to form 9765 bp FCTR3e (also referred to as 10129612.0.258). An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8408-8410. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3e. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

Table 3G. Encoded FCTR3e 5'end nucleotide sequence (SEQ ID NO:11).

 $\tt CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGATTCTGCTACAACTATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAA$ 

In yet another embodiment another FCTR3a homolog, FCTR3f (also referred to as 10129612.0.352) was found having the 9729bp sequence shown in Table 3H. An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8382-8384. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3G, and the start and stop codons are in bold letters.

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#### Table 3H. Encoded FCTR3f nucleotide sequence (SEQ ID NO:12).

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA TTCTGCTACAACTATGACATCCATTTCTCCCACTTCAGACAGGATGAATACAAGGTGGCAAAGTGACAAGTGCCAAAAC 10 TGACCAGAGGACGCTGTGGCAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACAG AAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCT CATCCACCGGGAGTCAGATGAGTTTCCTAGACAAGGAACCAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCC CACACCGAAGCGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCC 15 GACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCT GTCCAGTCGTGAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCA  $\tt TTCCACCTACATCCTCGCCTAGTCTCCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCAG$ ATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCCAGATGAGGAATTCTCCCCCCAATTCATACCT 20  $\tt CTCTCCCACCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAAT$ CGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACACCACAGAGTCCGTTCAGCTTCAGGACAG CTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCA TCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGÇCATTGCCGCGGC 25 CCTCCTCTTGGCTATTTTGCTGGCGTATTTCATAGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAG TTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCATGCCCA GTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGA  $\tt CCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGAAAAA$ 30 GACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGA GTGGGAATGGACAATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCCCATGAAT CAGTGCATCGATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTGTGTCTGCTCTGCTGGCTACAAAGGCGA GCACTGTGAGGAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCC 35 GACACGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGTGGCAC TCACGGCGTCTGCATCGGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACC CCCGCTGCATTGAGCATGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATT GATGGCTGCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGGCAGTGTCTCTGCCAGACCGG 40 CTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCCTGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGG ATTGTTTGGACCCTGACTGCTGCAGTCAGCCTGTCAGAACAGCCTGCTGCCGGGGGTCCCGGGACCCACTGGAC GAACTCCCCTGGTCGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCACG 45 GTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTGGTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACC  ${\tt CCCATCGTGCCTGAGACCCAGGTTCTTCATGAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTC}$ TAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAACCTCATTAGGGTTCACC 50 CAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCC TAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAAACCAGTTCCTGACCCAGCAG 55 GCATCTTTCCCTCTGGAAATGTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCCAGCACAC AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAA GTCTCTGAGTGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATG AAGCCCGCTGCGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 60 CTCATGTACTTTGTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGA  $\tt CCTCACTGCCGTCCGGCCGCTGAGCTGGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCCAACAGACCTTG$ CTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC

GGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTC TACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT TGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGA 5 TGGTACCATTTACATTGCAGACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCA ACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC TTCCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCAGATCATCACCCTCACCG TGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG 10 GCGCCCACGGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTG ATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTACAAGATCAAGTTCGGAACAGC  ${\tt CCTAGCGGGCACCATCACCCCCCACCATTGGACGCTGCCAACATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGT$ 15 GGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG TCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGA GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAACGTCAGTATATATTTGA 20 GTATGACTCCTCTGACCGCCTCCTTGCCGTCACCATGCCCAGCGTGGCCCGGCACAGCATGTCCACACACCTCCATCG GCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG AAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGA CAGTACCGCCGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCT GCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC 25 AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCCGTCATAAGTGAGACTCCCCTCCCCGT TGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACC AGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAAACTGGGGCC CTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGA 30 TATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGG GTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAGGCCAGCGGGTGGAGTGTCCAGTACC GCTATGATGGCGTAGGACGGCGGCTTCCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCT 35 CTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGCTGTTTCAGCA TCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATG AGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCTGTATATGTTCA AGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGA 40 TTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCCCTATGAATTGTCAGAGAG AAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACCACCCATC ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCG CAAGGTGGCATCTGTGCTGAACACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACT 45 TTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGGTG AACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTCACGAACATTGAGTTCCAGTACTCCAC GGCGAGAAGCAGCTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGGGATATTACGTGCTTCCCGTGGAGCAATACCC 50 AGAGCTTGCAGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGG**TAA**CAAAATAATCTGCTGC <u>CATTCCTTGTCTGAATGGCTCAGCAGGAGTAACTGTTATCTCCTCTCTAAGGAGATGAAGACCTAACAGGGGCACTGCG</u> GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCC <u>TGTTCCAAGTTCCCCTAAAATATGACCCACTTGTTCTGGGTCTACGCAGAAAAGAGACGCAAAGTGTCCAAAAGGAACAA</u> 55 <u>CGTCACCAGACCAGCTGCGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAGCAAATA</u> <u>CTGGAAATACTTTTTAAAGAAAAAAAAAACATGAGGGAATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCAT</u> 60 <u>ATGGTGGCTATAATCACTACAGATAAATTTCATACTCTTTTGTCTTTTGGAGATTCCATTGTGGACAGTAATACGCAGTTA</u> <u>CAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGTATCAGTTTCGGTAGAGGTGCAGCATCGTGACACTTTTGCTAAC</u> AGGTACCACTTCTGATCACCCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTTAAAATTATTAGTGTGT TTGTTTGGTCCAGAAACTGAGACAATCACATGACAGTCACCACGAGGAGAAAATTTAAAAAATAAAAATAAAAACAAA 65 AAAAATTTTAAAAAATTAAAAAAACAAAAATAAAGTCTAATAAGAACTTTGGTACAGGAACTTTTTTTGTAATATACATGTA TGAATTGTTCATCGAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAATTTATGGC AAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAAACTCCTGTG

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The FCTR3f polypeptide (SEQ ID NO:13) encoded by SEQ ID NO:12 is 2724 amino acid residues long and is presented using the one-letter code in Table 3I. This sequence differs from FCTR3b in that it is missing amino acids 758-766 from that polypeptide.

#### Table 3I. Encoded FCTR3f protein sequence (SEQ ID NO:13)

5 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTOKSYSSSETLKAYDHDSRMHYGNRVTDLIHRESDEFPRQGTNFTLAELGI CEPSPHRSGYCSDMGILHOGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDENGRPIP PTSSPSLLPSAOLPSSHNPPPVSCOMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNH  $\verb|TLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTV|$ YTPPPRLLPRNTFSRKAFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQI 10 HISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDG  $\verb|KDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDP| | Construction of the context of t$  ${\tt SCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNW}$ MGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHCTIDGCPDLCNGNGRCTLGQ NSWOCVCOTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVKSFYDRIKLLA 15 GKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWL PWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSL  $\tt LKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLILWEKRTALLQG$ FELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVG  $\tt DFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFD$ 20  ${\tt EARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMD}$ NSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINRLRQVTTNGEICL  ${\tt LAGAASDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNA}$  ${\tt DGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDG$  ${\tt NTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASYTVVQDQVRNSYQL}$ 25 CNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIR TEKIYDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYLDKSMV LLLOSOROYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKL SEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPV DLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTK 30 YTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNPGNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLL  ${\tt TRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAMESSSGEEYYVASDNTITH CONTROL OF STREET AND STRE$ GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLY MFKSNNPLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAFMALEGQV ITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGD LVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR

In a BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Mus musculus* odd Oz/ten-m homolog 2. It has 634 of 685 bases (92%) identical to bases 614-1298, 365 of 406 bases (89%) identical to bases 1420-1825, and 93 of 103 bases (90%) identical to bases 1823-1925 of *Mus musculus* odd Oz/ten-m homolog 2 (GenBank Acc: NM 011856.2) (Table 3J).

Table 3J. BLASTN of FCTR3a against *Mus musculus* odd Oz/ten-m homolog 2 (SEQ ID NO:62)

		SBJCT:		TCCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 233
	5	QUERY:		CAAATCATGGACACCCAACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCA 293
		SBJCT:	734	CAGATCATGGACACCCAACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCA 793
	10	QUERY:		TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACT 353
				CTGAGGCCCCCTCTCCCACCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCC 413
	15	QUERY: SBJCT:		CTGAGGCCCCTCTCCCACCCCTCACAACCACACCACCACCACCACC
		QUERY:	414	AACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473
	20	SBJCT:	914	
	20	QUERY:	474	GCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACAGCTGGGTGCTA 533
		SBJCT:	974	
	25	QUERY:	534	AACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACA 593
		SBJCT:	1034	AACAGTAACGTCCCACTGGAGACTCGGCACTTCCTTTTCAAAACGTCGTCTGGAAGCACA 1093
11.11 1.11 11.11 11.11	30	QUERY:	594	CCCTTGTTCAGCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCC 653
ij	30	SBJCT:	1094	CCCCTGTTCAGCAGCTCTTCTCCGGGATACCCTTTGACCTCAGGGACCGTTTATACACCA 1153
7, W. W. W.		QUERY:	654	CCGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCC 713
la k	35	SBJCT:	1154	CCACCCCGCCTGCTGCCACGGAATACATTCTCCAGGAAGGCCTTCAAGCTGAAGAAACCC 1213
Mark are		QUERY:	714	TCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTGCCGCGGCCCTCCTCTTG 773
# # # # # # # # # # # # # # # # # # #	40	SBJCT:	1214	TCCAAATACTGCAGTTGGAAATGTGCTGCCTGTCTGCCATCGCCGCCCCCCCC
11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		QUERY:	774	GCTATTTTGCTGGCGTATTTCATAG 798
and the second		SBJCT:	1274	GCCATTTTGCTGGCATATTTCATAG 1298
4m8	45	IDENT:	ITIES	80 BITS (242), EXPECT = E-132 = 365/406 (89%) LUS / PLUS
	50	QUERY:	797	AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 856
	<b>30</b> ,	SBJCT:	1420	AGTGCCCTGGTCATTGAAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479
		QUERY:	857	GGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAG
	55	SBJCT:	1480	GGTGACACAGGAAGTCCCACCAGGGGTGTTTTGGAGGTCCCAGATTCACATCAGTCAG
		QUERY:	917	CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAG 976
	60	SBJCT:	1540	TCAATTCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTTCGGTGTCTATATAAG 1599
		QUERY:	977	AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1036
		SBJCT:	1600	GAGAGGACTACCACCGTCTCATGCCCAGTATGACTTCATGGAACGCCTGGATGGA
	65	QUERY:	1037	GAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAA 1096
		SBJCT:	1660	GAAATGGAGCGTGGTCGAGTCGCCCAGGGAACGCCGGAGCATCCAGACTCTGGTGCAGAA 1719
	70	QUERY:	1097	TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1156

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SBJCT: 1720 CGAGGCTGTGTTTGTGCAGTACTTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779
    QUERY: 1157 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGAT 1202
               5
    SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGAT 1825
     SCORE = 125 BITS (63), EXPECT = 7E-26
     IDENTITIES = 93/103 (90%)
     STRAND = PLUS / PLUS
10
    QUERY: 1258 GATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCCGGGGTG 1317
              SBJCT: 1823 GATTCAGTGCAGGACTGTCCACGGAACTGTCACGGGAACGGTGAATGCGTGTCTGGACTG 1882
15
    QUERY: 1318 TGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAG 1360
              SBJCT: 1883 TGTCACTGTTTCCCAGGATTCCTAGGTGCAGACTGTGCTAAAG 1925
          In another BLASTN search it was found that the FCTR3a nucleic acid has homology to
20
    three fragments of Gallus gallus mRNA for teneurin-2. It has 541 of 629 bases (86%) identical
    to bases 502-1130, 302 of 367 bases (82%) identical to bases 1330-1696, and 87 of 103 bases
    (84%) identical to bases 1711-1813 of Gallus gallus mRNA for teneurin-2 (EMBL Acc:
    AJ245711.1) (Table 3K).
25
       Table 3K. BLASTN of FCTR3a against Gallus gallus mRNA for teneurin-2 (SEQ ID
                                    NO:63)
     >GI|6010048|EMB|AJ245711.1|GGA245711 GALLUS GALLUS MRNA FOR TENEURIN-2, SHORT SPLICE
     VARIANT (TEN2 GENE)
             LENGTH = 2496
30
     SCORE = 549 BITS (277), EXPECT = E-153
     IDENTITIES = 541/629 (86%)
     STRAND = PLUS / PLUS
35
     QUERY: 114
              GGTCGTCCCATTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGC 173
              SBJCT: 502
     QUERY: 174
              TCCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 233
40
              TCTCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAATACGTCCCAT 621
     SBJCT: 562
     QUERY: 234
              CAAATCATGGACACCAGCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCA 293
               45
     SBJCT: 622
              CAAATCATGGACACCAATCCTGACGAGGAGTTCTCTCCTAATTCATACCTACTAAGAGCA 681
              QUERY: 294
               SBJCT: 682
              TGTTCAGGGCCACAGCAGCAGCAGTGGCCCTTCAAACCATCACAGCCAGTCAACG 741
50
              CTGAGGCCCCTCTCCCACCCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCC 413
     QUERY: 354
               CTGAGGCCACCTCTCCCCCCTCTCACAACCACTCGCTGTCCCATCATCACTCGTCTGCC 801
     SBJCT: 742
55
              AACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473
     QUERY: 414
               SBJCT: 802
              AACTCCCTCAACAGGAACTCGCTCACCAACCGCCGCAACCAGATCCACGCGCCTGCTCCC 861
              GCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACAGCTGGGTGCTA 533
     QUERY: 474
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SBJCT: 862 GCTCCCAATGACCTGCGACCACGCCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTC 921

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AACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACA 593
      OUERY: 534
              AACAGCAACGTGCCGCTGGAGACCAGGCATTTCTTGTTTAAGACATCTTCTGGAACGACT 981
      SBJCT: 922
  5
              CCCTTGTTCAGCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCC 653
      QUERY: 594
                 CCGCTGTTCAGTAGCTCTTCCCCTGGCTACCCACTGACCTCAGGAACAGTTTATACTCCA 1041
      SBJCT: 982
              CCGCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCC 713
 10
      QUERY: 654
              SBJCT: 1042 CCTCCCAGGCTGTTACCTAGAAATACATTTTCCAGGAATGCATTCAAGCTGAAAAAGCCC 1101
              TCCAAATACTGCAGCTGGAAATGTGCTGC 742
 15
               SBJCT: 1102 TCCAAGTATTGTAGCTGGAAATGTGCTGC 1130
       SCORE = 212 BITS (107), EXPECT = 4E-52
       IDENTITIES = 302/367 (82%)
 20
       STRAND = PLUS / PLUS
      QUERY: 819 AGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCGGGTAACACAAGAAGTCCCACCA 878
                                         SBJCT: 1330 AGCAGCATAGATAGTGGAGAAACAGAAGTTGGCCGCAAGGTCACCCAAGAGGTGCCCCCT 1389
  25
              GGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC 938
      QUERY: 879
               SBJCT: 1390 GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCCTGAAGTTCAACATA 1449
30
              TCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCAT 998
      QUERY: 939
fil
               SBJCT: 1450 TCCCTAGGGAAGGATGCTCTTTTCGGTGTTTATATAAGAAGAGGACTCCCACCATCACAT 1509
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t,
              35
               L.
      SBJCT: 1510 GCACAGTATGATTCATGGAACGCTTGGATGGAAAGAAATGGAGTGTGGTGGAATCC 1569
Ti,
      OUERY: 1059 CCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTAC 1118
                 40
      OUERY: 1119 CTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT 1178
7 ....
               1
      SBJCT: 1630 TTGGATGTGGGTTTGTGGCACCTGGCGTTTTACAATGATGGCAAGGACAAAGAAGTGGTC 1689
  45
      QUERY: 1179 TCCTTCA 1185
               SBJCT: 1690 TCCTTCA 1696
  50
       SCORE = 77.8 BITS (39), EXPECT = 1E-11
       IDENTITIES = 87/103 (84%)
       STRAND = PLUS / PLUS
      QUERY: 1258 GATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCCGGGGTG 1317
  55
               SBJCT: 1711 GATTCAGTGCAAGACTGTCCACGTAATTGTCATGGCAATGGCGAGTGTGTTTCTGGTGTC 1770
      QUERY: 1318 TGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAG 1360
               60
      SBJCT: 1771 TGCCACTGTTTTCCCGGATTTCATGGAGCAGATTGTGCTAAAG 1813
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In this search it was also found that the fragments of FCTR3bcd and e nucleic acids had homology to three fragments of *Homo sapiens* mRNA for KIAA1127 protein. It has 5537 of 5538 bases (99%) identical to bases 1-5538, 705 of 714 bases (98%) identical to bases 5609-

6322, and 176 of 176 bases (100%) identical to bases 6385-6560 of *Homo sapiens* mRNA for KIAA1127 protein (GenBank Acc: AB032953) (Table 3L).

## Table 3L. BLASTN of FCTR3b, c, d, and e against *Homo sapiens* KIAA1127 mRNA (SEQ ID NO:64)

5 >GI | 6329762 | DBJ | AB032953.1 | AB032953 HOMO SAPIENS MRNA FOR KIAA1127 PROTEIN, PARTIAL CDS LENGTH = 6560SCORE = 1.097E+04 BITS (5534), EXPECT = 0.010 IDENTITIES = 5537/5538 (99%) STRAND = PLUS / PLUS OUERY: 3267 CACCTTCTTTAGTGCTGCCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 3326 15 CACCTTCTTTAGTGCTGCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 60 SBJCT: 1 QUERY: 3327 TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAACTGC 3386 TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAACTGC 120 SBJCT: 61 20 QUERY: 3387 AGGGTACAAGTCACTGCAGAGATCACCATGACCCAGTCCACAGTGCCCCTGAACCTCAT 3446 AGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAACCTCAT 180 SBJCT: 121 25 OUERY: 3447 TAGGGTTCACCTGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCATTCCAGGCTTC 3506 TAGGGTTCACCTGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCATTCCAGGCTTC 240 SBJCT: 181 QUERY: 3507 TCCCAACCTGGCCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTA 3566 30 TCCCAACCTGGCCTACACCTTCATCTGGGACAGACAGATGCGTATGGCCAAAGGGTGTA 300 SBJCT: 241 OUERY: 3567 TGGACTCTCAGATGCTGTTGTGTCTGTCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 3626 35 TGGACTCTCAGATGCTGTTGTGTCTGTCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 360 SBJCT: 301 QUERY: 3627 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 3686 TCTCTGGGAGAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 420 SBJCT: 361 40 QUERY: 3687 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 3746 TGGCTGGTCCCTAGACAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 480 SBJCT: 421 45 OUERY: 3747 CACTGGGGAAAACCAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 3806 CACTGGGGAAAACCAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 540 SBJCT: 481 QUERY: 3807 TGGTCGCCGCCGGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 3866 50 TGGTCGCCGCGGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 600 SBJCT: 541 OUERY: 3867 GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 3926 55 GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 660 SBJCT: 601 QUERY: 3927 TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAA 3986 TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAA 720 SBJCT: 661 60 QUERY: 3987 AGAGTTTAAACATAGCAACACCCAGCACACAGTACTACTTGGCAGTGGACCCCGTGTC 4046 AGAGTTTAAACATAGCAACACCCAGCACACAGTACTACTTGGCAGTGGACCCCGTGTC 780 SBJCT: 721 65 QUERY: 4047 CGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAG 4106

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		SBJCT:	781		40
				TGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 41	
	5	SBJCT:		TGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGGAGTGTCT 90	
		QUERY:	4167	ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 42	226
	10	SBJCT:	901	ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGCAAGGCCATAGATGCAACCCTGATGAG	60
		QUERY:	4227	CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGAT 42	286
	15	SBJCT:	961	CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGAT 1	020
	13	QUERY:	4287	CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 43	346
		SBJCT:	1021	CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 1	080
	20	QUERY:	4347	CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCC 44	406
		SBJCT:	1081	CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCC 1:	140
	25	QUERY:	4407	AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCAT 4	466
	240	SBJCT:	1141	AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCAT 1:	200
===		QUERY:	4467	CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 4	526
14. 14. 14. 14. 14. 14. 14. 14. 14. 14. 14. 14.	30	SBJCT:	1201	CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 1:	260
		QUERY:	4527	AGTTCCTGGCATTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCTGGAGTCAGC 4	586
######################################	35	SBJCT:	1261	AGTTCCTGGCATTGACTCACTCAGCAAACTAGCCATTCACTCTGCCCTGGAGTCAGC 1:	320
		QUERY:	4587	CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 4	646
Ą.J		SBJCT:	1321	CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 1	380
dun's stand	40	QUERY:	4647	GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 4	706
24 24 25		SBJCT:	1381	GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 1	440
100 AMA	45	QUERY:	4707	CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTA 4	766
a la		SBJCT:	1441	CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTA 1	.500
		QUERY:	4767	CGCGACTGATGCCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCAT 4	826
	50	SBJCT:	1501	CGCGACTGATGCCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCAT 1	.560
		QUERY:	4827	TTACATTGCAGACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCCTGTTCT 4	886
	55	SBJCT:	1561	TTACATTGCAGACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCCTGTTCT 1	.620
		QUERY:	4887	TAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAA 4	946
		SBJCT:	1621	TAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAA 1	.680
	60	QUERY:	4947	CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 5	006
		SBJCT:	1681	CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGGAGTACTTGTACAATTT 1	.740
	65	QUERY:	5007	CACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCCTGAA 5	066
		SBJCT:	1741	CACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCCTGAA 1	.800
		QUERY:	5067	GATCCGTCGGGACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCAGATCAT 5	126
	70	SBJCT:	1801	GATCCGTCGGGACAGCAGTGCCATGCCCCGTCACCTCATGCCTGACAACCAGATCAT 1	.860

		QUERY:	5127	CACCCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCT	2186
	5	SBJCT:	1861	CACCCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCT	1920
	5	QUERY:	5187	TGGTCTCATGACCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG	5246
		SBJCT:	1921	TGGTCTCATGACCTATGATGCCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG	1980
	10	QUERY:	5247	ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCCTGACCAACGTGACGCCCCCAC	5306
		SBJCT:	1981	ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCCTGACCAACGTGACGCGCCCCAC	2040
	15	QUERY:	5307	GGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAA	5366
	13	SBJCT:	2041	GGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAA	2100
		QUERY:	5367	CTCCAACCGTGATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTA	5426
	20	SBJCT:	2101	CTCCAACCGTGATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTA	2160
		QUERY:	5427	CACAGTGGTACAAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG	5486
	25	SBJCT:	2161	CACAGTGGTACAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG	2220
		QUERY:	5487	GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCCTAGCGGG	5546
25				GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCCTAGCGGG	
	30	QUERY:	5547	CACCATCACCCCCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAA	5606
- 10 mg				CACCATCACCCCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAA	
es es	35			CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG	
11				CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG	
×Ę.	4.0			GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTCGGAC	
Herry June 18	40			GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTCGGAC	
Section Section		-		TGAAAAGATCTATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGACCAGGTGGG	
22	45			TGAAAAGATCTATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGACCAGGTGGG	
###				CCGCCCTTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT	
	50			CCGCCCTTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT  CAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGACACACAA	
	50			CAATGGGCGCCTGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACA	
				GCAAGGCCGCATCGTGTCCCGCATGTTCGCTGACGGGAAAGTGTGGAGCTACTCCTACCT	
	55			GCAAGGCCGCATCGTGTCCCCCATGTTCGCTGACGGGAAAGTGTGGAGGCTACTCCTACCT	
				TGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAACGTCAGTATATATTTGAGTATGACTC	
	60	~			
				CTCTGACCGCCTCCTTGCCGTCACCATGCCCAGCGTGGCCCGGCACAGCATGTCCACACA	
		~			
	65			CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCAT	
	70	OHERY.	6147	· ctttgactacaggaggacgccatcctgaagacctccttttttgggcaccggacgcca	6206

				CTTTGACTACAGTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCA 294	
	5	QUERY:	6207	GGTGTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 626	6
		SBJCT:	2941	GGTGTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 300	0
		QUERY:	6267	CGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 632	6
	10	SBJCT:	3001	CGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 306	0
		QUERY:	6327	GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 638	6
	15	SBJCT:	3061	GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 312	:0
	10	QUERY:	6387	CAGGTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 644	:6
		SBJCT:	3121	CAGGTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 318	0 0
	20	QUERY:	6447	CTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTTGACCTCTA 650	16
		SBJCT:	3181	CTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTTGACCTCTA 324	ŧ 0
	25	QUERY:	6507	CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 656	;6
		SBJCT:	3241	CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 330	0 (
44 11.14		QUERY:	6567	TGACATCAACCAGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCA 662	}6
74. 4m	30	SBJCT:	3301	TGACATCAACCAGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCA 336	50
R HOTH HOTH		QUERY:	6627	TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT 668	36
	35			TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT 342	
1985, 18"15 Tools, 18"15		QUERY:	6687	GCAATATGACAGCATGGGCAGGGTGATCAAGAGGGGGCCTAAAACTGGGGCCCTATGCCAA 674	16
₹				GCAATATGACAGCATGGCCAGGGTGATCAAGAGGGGGCCTAAAAACTGGGGCCCTATGCCAA 348	
Hand and	40	_		TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA 680	
HIND HING		SBJCT:	3481	TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA 354	10
13	45	~		TGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC 686	
gradi.				TGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC 360	
		QUERY:	6867	AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT 692	26
	50			AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT 366	
		-		CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT 698	
	55			CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT 372	
				CTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGTGGAG 704	
	60			CTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGGTGGAG 378	
	60	~		TGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCCTACAAGACCAACCTGGGCCA 71(	
				TGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCCTACAAGACCAACCTGGGCCA 384	
	65	~		CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA 71	
				CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA 39	
	<b>5</b> 0	QUERY:	7167	TCACTCCAACTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT 72:	26
	70	SBJCT:	3901	TCACTCCAACTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT 396	60

:	•	QUERY:	1221	GGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGC	7200
	5	SBJCT:	3961	GGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGC	4020
		QUERY:	7287	TGTGTTCAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGAT	7346
		SBJCT:	4021	TGTGTTCAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGAT	4080
	10	QUERY:	7347	TTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA	7406
		SBJCT:	4081	TTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA	4140
	15	QUERY:	7407	CCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG	7466
		SBJCT:	4141	CCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG	4200
		QUERY:	7467	GACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT	7526
	20	SBJCT:	4201	GACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT	4260
		QUERY:	7527	GTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC	7586
	25			GTATATGTTCAAGAGCAACCAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC	
		QUERY:	7587	AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTT	7646
2 E		SBJCT:	4321	AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTT	4380
M. H. St.				CCCGAGAGCCAAAATGTATTTCGTGCCTCCTCCCTATGAATTGTCAGAGAGTCAAGCAAG	
75 24 27				CCCGAGAGCCAAAATGTATTTCGTGCCTCCTCCCTATGAATTGTCAGAGAGTCAAGCAAG	
	35	~		TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT	
Marie Arres				TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT	
===				CATGGCTCTGGAAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC	
With Minds				CATGGCTCTGGAAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC	
man day dam		-		AGGTCACTGGTTTGCCACCACCACCACCATCATTGGCAAAGGCATCATGTTTGCCATCAA	
100 M	45			AGGTCACTGGTTTGCCACCACCACCACCATCATTGGCAAAGGCATCATGTTTGCCATCAA	
gŠ.				AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC	
	<b>50</b>			AGAAGGCCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC	
	50		-	ATCTGTGCTGAACACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA	
				ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA	
	55			CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC	
				CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC	
	60			CATCGGCCGCAAGGTGCTAGAGAGGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCT	
	00			CATCGGCCGCAAGGTGCTAGAGAGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCT	
				GGTCAACGGCAGGACTCGAAGGTTCACGAACATTGAGTTCCAGTACTCCACGCTGCTGCT	
	65			GGTCAACGGCAGGACTCGAAGGTTCACGAACATTGAGTTCCAGTACTCCACGCTGCTGCT	
		_		CAGCATCCGCTATGGCCTCACCCCCGACACCCTGGACGACGAGAGAGA	
	70			CAGCATCCGCTATGGCCTCACCCCGACACCCTGGACGAAGAGAGAG	
	111		0/4/	ACIDICALIAN (1997)	0.00

		SBJCT: 4		
			3307 CGGGAGAGAGGGGAGCCGCCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGG 8366	
	5	SBJCT: 5		
		QUERY: 8	3367 GCGCGTGCAAGGGTACGAGGGATATTACGTGCTTCCCGTGGAGCAATACCCAGAGCTTGC 8426	
	10	SBJCT: 5	5101 GCGCGTGCAAGGGTACGAGGGATATTACGTGCTTCCCGTGGAGCAATACCCAGAGCTTGC 5160	
		QUERY: 8	8427 AGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAA 8486	
	15	SBJCT: !	5161 AGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAA 5220	
			8487 TAATCTGCTGCCATTCCTTGTCTGAATGGCTCAGCAGGAGTAACTGTTATCTCCTCTCCT 8546	
			5221 TAATCTGCTGCCATTCCTTGTCTGAATGGCTCAGCAGGAGTAACTGTTATCTCCTCTCT 5280	
	20		8547 AAGGAGATGAAGACCTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCA 8606	
			5281 AAGGAGATGAAGACCTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCA 5340	
	25	_	8607 AGAAAGCTCACATTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCCCTCATCCTG 8666	
			8667 AAGTAGACTAAAGCCCGGCTGAAAATTCCGAGGAAAACAAAACAAAC	
Man Hall	30			
19 15 14 15 15 15 15 15 15 15 15 15 15 15 15 15			8727 GACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTGTTCTGGGTCTACGCAG 8786	
***		SBJCT:		
1.	35	QUERY:	8787 AAAAGAGACGCAAAGTGT 8804	
Mark Mark		SBJCT:		
Mark Street House	40	IDENTI	1362 BITS (687), EXPECT = 0.0 TIES = 705/714 (98%) = PLUS / PLUS	
<b>1</b> 00	45	QUERY:	8875 CACGGACCGATAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCA 8934	
Park	40	SBJCT:	5609 CACGGACCGATAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCA 5668	
		QUERY:	8935 CTCATTCACATGTGAGCGACACGCAGACATCCGCGAGGGCCAGCGTCACCAGACCAGCTG 8994	
	50		5669 CTCATTCACATGTGAGCGACACGCAGACATCCGCGAGGGCCAGCGTCACCAGACCAGCTG 5728	
			8995 CGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAGCAA 9054	
	55		5729 CGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAGCAA 5788	
		~	9055 ATACAGGTGCATTTAAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCCTGGGGAGGGG 9114	
	60		9115 GGATAAAAGAGGAGGAGTGAGCACTGGAAATACTTTTTAAAGNNNNNNNNNN	
	00	~		
	65	52001.		
		QUERY:	9175 ATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCATCCAGCACTTAACTCTCA 9234	
	65	~	9175 ATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCATCCAGCACTTAACTCTCA 9234	
	65	SBJCT:		

la.

40 11 In this search it was also found that the FCTR3bcd and e nucleic acids had homology to five fragments of *Mus musculus* mRNA for Ten-m2. It has 5498 of 6108 bases (90%) identical to bases 2504-8610, 1095 of 1196 bases (91%) identical to bases 103-1298, 1000 of 1088 bases (91%) identical to bases 1420-2540, 81 of 89 bases (91%) identical to bases 8655-8743, and 30 of 32 bases (93%) identical to bases 7-38 of *Mus musculus* mRNA for Ten-m2 (Table 3M).

# Table 3M. BLASTN of FCTR3b, c, d, and e against *Mus musculus* mRNA for Ten-m2 Mrna (SEQ ID NO:65)

```
>GI|4760777|DBJ|AB025411.1|AB025411 MUS MUSCULUS MRNA FOR TEN-M2, COMPLETE CDS
45
            LENGTH = 8797
     SCORE = 7263 BITS (3664), EXPECT = 0.0
     IDENTITIES = 5498/6108 (90%), GAPS = 1/6108 (0%)
50
     STRAND = PLUS / PLUS
     QUERY: 2578 GATGGCTGCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2637
              SBJCT: 2504 GATGGCTGCCCTGATTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2563
55
     OUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCC 2697
               SBJCT: 2564 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCCATGGAAACCTCC 2623
60
     QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGC 2757
```

		SBJCT:	2624	TGCGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGACTGCCTGACTGC 2883
		-		TGCCTGCAGTCAGCCTGTCAGAACAGCCTGCTCTGCCGGGGGTCCCGGGACCCACTGGAC 2817
		-		ATCATTCAGCAGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAG 2877
	10			CTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGC 2937
				CTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGACAACCCCTTCAATAGCAGC 2863
	15			TTGGTTTCTCTCATCCGAGGCCAAGTAGTAACTACAGATGGAACTCCCCTGGTCGGTGTG 2997
	13			
		OUERY:	2998	AACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCCATCACCCGCCAGGATGGCACG 3057
	20			
		QUERY:	3058	TTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGC
	25	SBJCT:	2984	
		QUERY:	3118	ATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTG 3177
5 H H H H H	30	SBJCT:	3044	
Ti.	50	QUERY:	3178	GTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3237
### H###		SBJCT:	3104	GTAATGAAGACCGAGGAAAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCA 3163
-	35	QUERY:	3238	GATCCAATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCCTGGGCAGAAT 3297
		SBJCT:	3164	GATCCAATCATCTCCTCTCTCTCTCTCTCTCTCACCTTCTCCACCCTCCCCTCCCTCCAAC 3223
*	40	QUERY:	3298	CCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTG 3357
med dung	40	SBJCT:	3224	CCCATTGTGCCTGAGACCCAGGTTCTTCATGAAGAAATTGAGCTCCCTGGTACCAATGTG 3283
100		QUERY:	3358	AAACTTCGCTATCTGAGCTCTAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3417
	45	SBJCT:	3284	AAGCTCCGTTATCTCAGCTCTAGAACTGCAGGGTATAAGTCGCTGCTGAAGATCACCATG 3343
•		QUERY:	3418	ACCCAGTCCACAGTGCCCCTGAACCTCATTAGGGTTCACCTGATGGTGGCTGTCGAGGGG 3477
	50	SBJCT:	3344	ACGCAGTCCACAGTGCCCTTGAACCTCATCAGGGTTCACTTGATGGTTGCTGTAGAGGGG 3403
	50	QUERY:	3478	CATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC 3537
		SBJCT:	3404	CATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTAGCCTACACATTCATCTGGGAC 3463
	55	QUERY:	3538	AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTC
		SBJCT:	3464	
	60	QUERY:	3598	TTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAG 3657
	00	SBJCT:	3524	TTTGAATATGAGACCTGCCCCAGTCTCATCCTGTGGGAGAAAAGGACAGCCCTGCTTCAG 3583
		QUERY:	3658	GGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTC 3717
	65	SBJCT:	3584	
		QUERY:	3718	AATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAAACCAGTTCCTGACCCAGCAG 3777
	70	SBJCT:	3644	

		QUERY:	3778	CCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCCGGAGCATTTCCTGTCCCAGC	3837
		SBJCT:	3704	CCTGCCATCATCACGAGCATCATGGGCAACGGTCGCCGCAGAAGCATCTCCTGTCCCAGC	3763
	5	QUERY:	3838	TGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATC	3897
		SBJCT:	3764	TGCAATGGCCTTGCTGAAGGCAACAAACTGTTAGCCCCTGTGGCCCTGGCTGTGGGGATC	3823
	10	-		GATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGACGCATCTTTCCCTCTCGAAAT	
				GATGGGAGCCTCTTTGTTGGTGACTTCAACTATATCCGGCGCATCTTTCCCTCTCGAAAT .	
				GTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC	
	15			GTGACCAGTATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAGCCCAGGACAC	
				AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGC	
	20			AAGTACTACTTGGCTGTGGACCCCGTGACTGGCTCACTCTACGTCTCTGACACCAACAGT	
				AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAGACCTGGCTGG	
	25			CGCCGAATCTACCGAGTCAAGTCTCTGAGCGGAGCCAAAGACCTGGCTGG	
	23			GTTGTGGCAGGACGGAGAGCAGTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGA	
***				GGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG	
	30				
				CTCATGTACTTTGTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCC	
L.	35	SBJCT:	4184		4243
Sent Mer.		QUERY:	4318	ACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATG	4377
11 11 16 th	40	SBJCT:	4244	ACCCTGCTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTGACTCGAGCATG	4303
Mary San	40	QUERY:	4378	GATGTAGCCCAGGTTCGTCTGGAGTGGCCAACAGACCTTGCTGTCAATCCCATGGATAAC	4437
THE STATE OF THE S		SBJCT:	4304	GACGTGGCCAGGTCCGTCTAGAATGGCCGACAGACCTCGCCGTCAACCCCATGGACAAC	4363
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	45	QUERY:	4438	TCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC	4497
		SBJCT:	4364	TCCCTGTACGTTCTGGAGAACAACGTCATCCTGCGGATCACGGAGAACCACCAGGTCAGC	4423
	50	QUERY:	4498	ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTC	4557
				ATCATCGCGGGACGGCCTATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAA	
	<i></i>			CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC	
	55			CTCGCCATCCACTCTGCGCTGGAATCAGCCAGCGCCATTGCCATTTCTCACACTGGGGTG	
		*******		CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC	
	60			GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT	
	65			TGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCCCATCA	
				TCCTTAGCTGTAGCTCCAGATGGTACCATTTACATTGCAGACCTTGGAAATATTCGGATC	
	70			51	1596
				▼ <del>-</del>	

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		SBJCT:	4724	TCCTTAGCCGTGGCTCCGGATGGCACCATCTACATTGCAGACCTTGGGAATATCCGGATC	4783
	5			AGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCC	
	3				
				CCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC	
	10			CTGGTGACAGGGGAGTACTTGTACAATTTCACATATAGTACTGACAATGATGTCACTGAA	
		-			
	15	QUERY:	5038	$\tt TTGATTGACAATAATGGGAATTCCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGT$	5097
		SBJCT:	4964		5023
	20	QUERY:	5098	CACCTGCTCATGCCTGACAACCAGATCATCACCCTCACCGTGGGCACCAATGGAGGCCTC	5157
	20	SBJCT:	5024		5083
		QUERY:	5158	AAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG	5217
	25			AAAGCCGTGTCCACTCAGAACCTGGAGCTGGGCCTCATGACTTATGATGGGAACACTGGA	
****		QUERY:	5218	CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAA	5277
100 SCH	30	SBJCT:	5144	CTCCTAGCCACCAAGAGTGATGAAACCGGATGGACAACTTTTTATGACTATGACCACGAG	5203
Įij.	50	QUERY:	5278	GGCCGCCTGACCAACGTGACGCGCCCCACGGGGGTGGTAACCAGTCTGCACCGGGAAATG	5337
10 10 10 10 10 10 10 10 10 10 10 10 10 1		SBJCT:	5204	GGCCGTCTGACCAATGTGACCCGCCCCACGGGCGTGGTGACCAGTCTGCACCGGGAAATG	5263
	35	QUERY:	5338	GAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTGATGATGACGTCACTGTCATC	5397
Ti.		SBJCT:	5264	GAGAAATCTATCACCATTGACATTGAGAACTCCAACCGGGATGATGACGTCACTGTGATC	5323
*	40	QUERY:	5398	ACCAACCTCTCTCAGTAGAGGCCTCCTACACAGTGGTACAAGATCAAGTTCGGAACAGC	5457
mil Hall		SBJCT:	5324	ACCAACCTCTCCGTGGAGGCCTCCTATACAGTGGTACAAGATCAAGTGCGAAACAGC	5383
THE STATE		QUERY:	5458	TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGC	5517
ration of the same	45	SBJCT:	5384		5443
a in		QUERY:	5518	TTCCACAGCGAGCCCCATGTCCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAAC	5577
	50	SBJCT:	5444		5503
		QUERY:	5578	ATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGTGGCGCCTAAGAAAGGAACAG	5637
		SBJCT:	5504	ATCTCTCTGCCCATGGAGAATGGCCTGAACTCCATCGAGTGGCGCCTGAGGAAGGA	5563
	55	QUERY:	5638	ATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG	5697
		SBJCT:	5564		5623
	60	QUERY:	5698	${\tt TCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTC}$	5757
	60	SBJCT:	5624		5683
		QUERY:	5758	ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCCTTCCTCTGGCTGCCCAGCAGCGG	5817
	65	SBJCT:	5684		5743
		QUERY:	5818	CTGGCAGCTGTCAACGTGTCATACTTCTTCAATGGGCGCCTGGCTTGGGCTTCAGCGTGGG	5877
	70	SBJCT:	5744		5803

		QUERY:	5878	GCCATGAGCGAGAGACATCGACAAGCAAGGCCGCATCGTGTCCCGCATGTTCGCT	5937
		SBJCT:	5804	GCCATGAGCGAGAGACAGACATTGACAAGCAAGGCCGGATCGTGTCCCGCATGTTCGCC	5863
	5	QUERY:	5938	GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCCTCCTGCTTCAGAGC	5997
		SBJCT:	5864	GACGGGAAAGTCTGGAGTTATTCCTATCTTGACAAGTCCATGGTCCTTCTGCTACAGAGC	5923
	10	QUERY:	5998	CAACGTCAGTATATATTTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTCACCATGCCC	6057
		SBJCT:	5924	CAACGTCAGTACATATTTGAATATGACTCCTCCGATCGCCTCCACGCAGTCACTATGCCC	5983
		QUERY:	6058	AGCGTGGCCCGGCACAGCATGTCCACACACCCTCCATCGGCTACATCCGTAATATTTAC	6117
	15	SBJCT:	5984	AGTGTCGCCCGGCACAGCATGTCCACGCACACCTCCATTGGTTACATCCGAAACATTTAC	6043
		~		AACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG	
	20			AACCCACCGAAAGCAATGCATCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTA	
				AAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAG	
				AAGACATCTTTCTTGGGCACTGGGCGCCAGGTGTTCTACAAGTATGGAAAACTCTCCAAG	
	25			TTATCAGAGATTGTCTACGACAGTACCGCCGTCACCTTCGGGTATGACGAGACCACTGGT	
f'''g 11 12 13 14 14 14 14 14 14 14 14 14 14 14 14 14				TTATCAGAGATAGTCTACGACAGCACAGCCGTCACCTTTGGGTATGACGAGACCACCGGT	
	30			GTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCTGCACCATCAGGTACCGGAAG	
3000 H 11				GTCCTGAAGATGGTCAATCTCCAAAGTGGGGGCTTCTCCTGTACCATCAGGTACCGAAAG	
1-5	35	~		ATTGGCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC	
The state of the s				AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATA	
Mark Start.				AGGTTTGACTACACCTATCACGACAACACTTCCGCATCGCAACCATCAAACCCGTCATT  AGGTTTGATTATACCTATCACGACAATAGCTTCCGCATTGCCAGCATCAAACCCGTCATT	
### ###	40			AGTGAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAA	
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1					
Story W. H.	45	QUERY:	6538	CACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACCAGATCATCACCACTGCCGTG	6597
in in					
	<b>~</b> 0	QUERY:	6598	ATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG	6657
	50	SBJCT:	6524	ATGACGCTTAGCAAGCACTTTGACACCCATGGGCGCATCAAGGAAGTGCAATATGAGATG	6583
		QUERY:	6658	TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAG	6717
	55	SBJCT:	6584	TTCCGGTCCCTCATGTACTGGATGACTGTGCAATATGACAGTATGGGTAGGGTCATCAAG	6643
		QUERY:	6718	AGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGG	6777
	60	SBJCT:	6644	AGGGAACTGAAACTAGGGCCCTATGCCAACACCACAAAGTACACCTATGACTATGACGGG	6703
	00	QUERY:	6778	GACGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGACCTGGCGCTACAGCTATGAC	6837
		SBJCT:	6704	GACGGCCAGCTCCAGAGTGTGGCCGTCAATGACCGGCCTACCTGGCGCTATAGCTATGAC	6763
	65	QUERY:	6838	CTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGCGCCTCATGCCCTTGCGC	6897
		SBJCT:	6764	CTCAATGGGAACCTGCACCTTCTAAACCCAGGAAACAGTGCTCGCCTCATGCCCTTACGC	6823
	70	QUERY:	6898	TATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGAT	6957

		SBJCT:	6824	TATGACCTCCGTGACCGGATAACCAGGCTAGGGGACGTGCAGTACAAAATCGATGACGAT	883
				GGCTATCTGTGCCAGAGAGGGTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACA	
				GGCTATTTGTGCCAGAGAGGGTCAGACATCTTTGAATACAACTCCAAGGGCCTTCTGACG	
				AGAGCCTACAACAAGGCCAGCGGGTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGG	
1	.0	SBJCT:	6944	AGAGCATACAACAAGGCCAGCGGATGGAGCGTGCAGTACCGCTATGACGGAGTGGGCCGC	7003
•		QUERY:	7078	CGGGCTTCCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC	7137
		SBJCT:	7004	CGGGCTTCCTACAAGACCAACCTGGGCCACCACCTACAGTACTTCTACTCCGACCTCCAC	7063
1	.5	QUERY:	7138	AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTAC	7197
		SBJCT:	7064		7123
_	20	QUERY:	7198	TACGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTT	7257
2	20	SBJCT:	7124		7183
		QUERY:	7258	GCCTCTGATAACACAGGGACTCCTCTGGCTGTTTCAGCATCAACGGCCTCATGATCAAA	7317
2	25	SBJCT:	7184	GCCTCAGACAACACGGGGACCCCTCTGGCTGTACAGTATCAATGGCCTCATGATCAAG	7243
		QUERY:	7318	CAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATG	7377
	20	SBJCT:	7244		7303
Full.	, U	QUERY:	7378	GTCATTGGCTTCCATGGGGGACTCTATGACCCCCTGACCAAGCTGGTCCACTTCACTCAG	7437
### ### ### ####		SBJCT:	7304		7363
kak 3	35	QUERY:	7438	CGTGATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAAC	7497
And State		SBJCT:	7364	CGTGATTATGACGTGCTGGCAGGACGTGGACGTCCCCCGACTACACCATGTGGAGGAAC	7423
e En 2	40	QUERY:	7498	GTGGGCAAGGAGCCGGCCCCTTTAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGC	7557
300	. •	SBJCT:	7424	GTGGGCAAGGACCAGCCCCTTCAACCTGTACATGTTCAAGAACAACCATCCTCTGAGC	7483
Harth gards		QUERY:	7558	AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGA	7617
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	45	SBJCT:	7484	AATGAGCTGGACTTAAAGAACTACGTGACAGACGTGAAGAGCTGGCTTGTGATGTTTGGA	7543
£		QUERY:	7618	TTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCT	7677
	50	SBJCT:	7544	TTTCAGCTCAGCAACATCATTCCTGGATTCCCGAGAGCCAAAATGTATTTTGTGCCTCCC	7603
•		QUERY:	7678	CCCTATGAATTGTCAGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAA	7737
		SBJCT:	7604	CCCTATGAACTGTCAGAGAGTCAAGCAAGCGAGAACGGACAGCTCATTACAGGTGTCCAG	7663
,	55	QUERY:	. 7738	CAGACAACAGAGAGACATAACCAGGCCTTCATGGCTCTGGAAGGACAGGTCATTACTAAA	7797
		SBJCT:	7664	CAGACAACTGAGAGGCCATAACCAGGCCTTCCTGGCTCTGGAAGGACAGGTCATCACTAAA	7723
	60	QUERY:	7798	AAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACCACCCATC	7857
·	00	SBJCT:	7724	AAGCTCCATGCCAGCATCCGAGAGAAAGCAGGCCACTGGTTTGCTACCACCACCACCCATC	7783
		QUERY:	7858	ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGC	7917
1	65	SBJCT:	7784	ATCGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACAGGAGTGTCTAGC	7843
		QUERY:	7918	ATCGCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACCTGGAC	7977
,	70	SBJCT:	7844		7903
	70				

		_		AAGATGCACTACAGCATCGAGGGCAAGGACACCCACTTTTGTGAAGATTGGCTCAGCC	
		SBJCT:	7904	AAGATGCACTACAGCATCGAGGGCAAGGACACACTACTTTGTGAAGATCGGCGCCGCG	7963
	5			GATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGGTG	
				GATGGTGACCTGGTCACGCTAGGAACCACCATTGGGCGCAAGGTGCTGGAGAGTGGGGTG	
	10			AACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTCACGAAC	
		SBJCT:	8024	AACGTGACGGTGTCACAGCCCACGCTGCTGGTGAATGGCAGGACTCGAAGGTTCACCAAC	8083
		_		ATTGAGTTCCAGGTGCTGCTGCTCAGCATCCGCTATGGCCTCACCCCCGACACC	
	15			ATTGAGTTCCAGTACTCCACGCTGCTGCTCAGTATCCGCTACGGCCTCACCCCCGACACG	
				CTGGACGAAGAGAGGCCCGCGTCCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCC	
	20			CTGGACGAAGAAAAGGCCCGCGTCCTGGACCAAGCGGGACAGAGAGCCCTGGGTACTGCC	
		-		TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCGCC	
	0.5			TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGAGAGAGAG	
	25			GGCGAGAAGCAGCATCTGAGCACCGGGCGCGTGCAAGGGTACGAGGGATATTACGTG	
5				GGCGAGAAGCAGCAACTCCTGAGCACGGGACGGGTACAAGGTTATGAGGGCTATTACGTA	
T.	30			CTTCCCGTGGAGCAATACCCAGAGCTTGCAGACAGTAGCAGCAACATCCAGTTTTTAAGA	
Hande offered				CAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGCCATTCCTTGTCTGAATGGCT	
10 m	35			CAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGCCACCTTCTCTGGGTGGCT	
Mary Mary	55			CAGCAGGAGTAACTGTTATCTCCTCTCTAAGGAGATGAAGACCTAACAGGGGCACTGCG	
28					
Many many	40			GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT	
Hart mil		SBJCT:	8503		8562
1	45	QUERY:	8638	ACTGTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGGC 8685	
1 = 1		SBJCT:	8563		
	50			70 BITS (792), EXPECT = 0.0	
	50			= 1095/1196 (91%) LUS / PLUS	
		QUERY:	270	ATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGGACGCTGTGG	329
	55	SBJCT:	103	ATCTGGAATAATGGATGTAAAGGACCGGCGACATCGCTCTTTGACCAGGGGACGGTGTGG	162
		QUERY:	330	CAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACA	389
	60	SBJCT:	163	CAAAGAGTGTCGCTACACCAGCTCCTCTCTGGACAGTGAGGACTGCCGTGTGCCCACTCA	222
		QUERY:	390	GAAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTA	449
		SBJCT:	223	GAAGTCCTACAGTTCCAGTGAGACCTTGAAGGCTTATGACCATGACAGCAGAATGCACTA	282
	65	QUERY:	450	TGGAAACCGAGTCACAGACCTCATCCACCGGGAGTCAGATGAGTTTCCTAGACAAGGAAC	509
		SBJCT:	283	TGGAAACCGAGTCACAGACCTGGTGCACCGGGAGTCCGATGAGTTTTCTAGACAAGGGAC	342
	70	QUERY:	510	CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG	569
				55	15966

15966-697

	SBJCT:	343	AAACTTCACCCTGGCAGAATTGGGAATCTGCGAGCCCTCCCCACACCGAAGTGGTTACTG 402
5	QUERY:		CTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTC 629
	OUERY:	630	CGACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAA 689
10	SBJCT:		
10	QUERY:	690	ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAAACTCGGCCCTTACCCTGACTGA
	SBJCT:	523	
15	QUERY:	750	TGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTACATCCTCGCC 809
	SBJCT:	583	
20	QUERY:	810	TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 869
20	SBJCT:	643	
	QUERY:	870	GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCCTGATGAGGA 929
25	SBJCT:	703	
	QUERY:	930	ATTCTCCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGGCCCCAGCAAGCCTCCAGCAG 989
	SBJCT:	763	
¥130	QUERY:	990	TGGCCCTCCGAACCACACCACTCGACTCTGAGGCCCCCTCTCCCACCCCCTCACAA 1049
200 m m m m m m m m m m m m m m m m m m	SBJCT:	823	TGGCCCTCCAAACCACCACAGCCAGTCAACACTGAGGCCCCCTCTGCCACCCCCCTCATAA 882
1 35 1 35	QUERY:	1050	CCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109
200 S	SBJCT:	883	CCACACCTGTCCCACCACCACTCCTCGGCCAACTCCCTCAACAGGAACTCACTGACCAA 942
£ 40	QUERY:	1110	TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGA 1169
	SBJCT:	943	TCGGCGGAGTCAAATCCACGCCCAGCTCCTGCGCCCAACGACCTGGCCACCACCCCAGA 1002
STATE CANTE	QUERY:	1170	GTCCGTTCAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCCGGCA 1229
☐ 45	SBJCT:	1003	GTCTGTTCAGCTCCAGGATAGCTGGGTGCTGAACAGTAACGTCCCACTGGAGACTCGGCA 1062
•	QUERY:	1230	CTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCAGCAGCTCTTCCCCGGGATA 1289
50	SBJCT:	1063	CTTCCTTTTCAAAACGTCGTCTGGAAGCACCCCTGTTCAGCAGCTCTTCTCCGGGATA 1122
	QUERY:	1290	CCCTTTGACCTCAGGAACGGTTTACACGCCCCGCCCCGC
	SBJCT:	1123	CCCTTTGACCTCAGGGACCGTTTATACACCACCCCCGCCTGCTGCCACGGAATACATT 1182
55	QUERY:	1350	CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGC 1409
	SBJCT:	1183	CTCCAGGAAGGCCTTCAAGCTGAAGAAACCCTCCAAATACTGCAGTTGGAAATGTGCTGC 1242
60	QUERY:	1410	CCTCTCCGCCATTGCCGCGGCCCTCCTCTTGGCTATTTTGCTGGCGTATTTCATAG 1465
	SBJCT:	1243	CCTGTCTGCCATCGCCGCCGCCCTCCTCTTGGCCATTTTGCTGGCATATTTCATAG 1298
65	IDENT	ITIES	55 BITS (734), EXPECT = 0.0 S = 1000/1088 (91%), GAPS = 3/1088 (0%) PLUS / PLUS
	QUERY:	1464	AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523
70	SBJCT:	1420	AGTGCCCTGGTCATTGAAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479

		~		GGTAACACAAGAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAG	
				GGTGACACAGGAAGTCCCACCAGGGGTGTTTTGGAGGTCCCAGATTCACATCAGTCAG	
				CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAG	
				TCAATTCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTTCGGTGTCTATATAAG AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA	
	10			AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGAAGGA	
				GAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAA	
	15	-			
				TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA	
	20	QUERY:	1824	TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTG	1883
		SBJCT:	1780		1839
	25	QUERY:	1884	TCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCCCGGGGTGTGTCACTGTTTCCCAGG	1943
\$# E-12		SBJCT:	1840	TCCACGGAACTGTCACGGGAACGGTGAATGCGTGTCTGGACTGTTCCCAGG	1899
Mr. H.	30	QUERY:	1944	ATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCCTGTGCAGTGGGAATGGACA	2003
100 de 10	30	SBJCT:	1900	ATTCCTAGGTGCAGACTGTGCTAAAGCTGCCTGCCCTGTACTGTGCAGCGGAAATGGACA	1959
	35 40			ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCC	
MF 4ff				GTATTCTAAAGGAACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGTGATGTGCC	
iii •				CATGAATCAGTGCATCGATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTG	
1900, 7700, 19 11 115, 1900, 1900,				TATGAACCAATGTATCGATCCTTCCTGTGGGGGCCATGGCTCCTGCATTGATGGGAACTG TGTCTGCTCTGC	
the stand		-		CGTGTGTGCTGCTGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCTAC	
# 15 m	45			CTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGG	
žub	15				
				TCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGCAGTGGGCATGGCACGTA	
	50	SBJCT:	2200		2259
		QUERY:	2304	CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT	2363
	55	SBJCT:	2260	CCTCCCTGACTCCGGCCTCTGCAGCTGTGATCCGAACTGGATGGGTCCCGACTGCTCTGT	2319
		QUERY:	2364	TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG	2423
	60	SBJCT:	2320	TGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG	2376
	00	QUERY:	2424	TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA	2483
		SBJCT:	2377	TGAAGAGGGCTGGACAGCCAGCTTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA	2436
	65			GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG	
		SBJCT:	2437	GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG	2496
	70	QUERY:	2544	CACCATTG 2551	

```
SBJCT: 2497 CACCATTG 2504
        SCORE = 105 BITS (53), EXPECT = 5E-19
        IDENTITIES = 81/89 (91%), GAPS = 1/89 (1%)
        STRAND = PLUS / PLUS
   5
       QUERY: 8711 AACGAATGAACAGACACACACACATGTTCCCAAGTTCCCCTAAAATATGACCCACTTG 8770
                  SBJCT: 8655 AACGAACGAATGAAAACACACACAAAATGTTTCAAGTTCCCCTAAAATATGACCCACTTG 8714
  10
       QUERY: 8771 TTCTGGGTCT-ACGCAGAAAAGAGACGCA 8798
                  SBJCT: 8715 TTCCGGGTCTAAGGCAGAAAAGAGACGCA 8743
       SCORE = 48.1 BITS (24), EXPECT = 0.093
  15
        IDENTITIES = 30/32 (93%)
        STRAND = PLUS / PLUS
       QUERY: 475 CACCGGGAGTCAGATGAGTTTCCTAGACAAGG 506
                 20
                 CACCGGGAGTCCGATGAGTTTTCTAGACAAGG 38
       SBJCT: 7
             In this search it was also found that the FCTR3bcd and e nucleic acids had homology to
(1) 25
        (91%) identical to bases 1440-2527 of Rattus norvegicus neurestin alpha (GenBank
```

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three fragments of Rattus norvegicus neurestin alpha. It has 5498 of 6132 bases (89%) identical to bases 2527-8658, 1081 of 1196 bases (90%) identical to bases 123-1318, 996 of 1088 bases Acc:NM 020088.1) (Table 3N).

### Table 3N. BLASTN of FCTR3b, c, d, and e against Rattus norvegicus Neurestin alpha mRNA (SEO ID NO:66)

```
>GI 9910319 REF NM 020088.1 RATTUS NORVEGICUS NEURESTIN ALPHA (LOC56762), MRNA
30
           LENGTH = 8689
     SCORE = 7129 BITS (3596), EXPECT = 0.0
     IDENTITIES = 5498/6132 (89%)
     STRAND = PLUS / PLUS
35
    QUERY: 2578 GATGGCTGCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2637
             SBJCT: 2527 GATGGCTGCCTGATTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2586
40
    QUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCC 2697
             SBJCT: 2587 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACCTCC 2646
    QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGC 2757
45
             SBJCT: 2647 TGCGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGACTGCCTGGACCCTGACTGC 2706
    QUERY: 2758 TGCCTGCAGTCAGCCTGTCAGAACAGCCTGCTCTGCCGGGGGTCCCGGGACCCACTGGAC 2817
             SBJCT: 2707 TGCCTCCAGTCAGCCTGTCAGAACAGCCTGCTCTGTCGGGGGGTCTCGGGACCCCTTGGAC 2766
50
    QUERY: 2818 ATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAG 2877
             SBJCT: 2767 ATCATTCAGCAAGGCCAGACAGACTGGCCTGCGGTGAAGTCCTTCTATGATCGTATCAAG 2826
55
    QUERY: 2878 CTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGC 2937
             SBJCT: 2827 CTCTTGGCAGGCAGGACACCACATCATTCCTGGAGACACCCCTTCAATAGCAGC 2886
60
    QUERY: 2938 TTGGTTTCTCTCATCCGAGGCCAAGTAGTAACTACAGATGGAACTCCCCTGGTCGGTGTG 2997
```

58

5		QUERY:	2998	AACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCACG 3057	
		SBJCT:	2947	AATGTGTCTTTTGTCAAGTACCCAAAATATGGCTACACCATCACTCGCCAGGACGGCACG 3006	
•	,	QUERY:	3058	TTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGC	
				TTTGACCTGATTGCCAATGGGGGCTCTGCCTTGACTCTTCACTTTGAGCGAGC	
1				ATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTG 3177	
				ATGAGCCGGGAGCGCACAGTATGGCCGCCGTGGAACAGCTTCTATGCCATGGACACCCTG 3126	
1	5	~		GTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3237	
				GTAATGAAGACGGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3186	
		-		GATCCAATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCCTGGGCAGAAT 3297	
2				GATCCGATCATCTCTCTCTCTCTCTCTCTCTCACCTTCTCAGCGCTTCCCCTGCGGCGAAC 3246	
				CCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTG 3357	
2	5			CCCATTGTGCCTGAGACCCAGGTTCTTCATGAGGAGATCGAGCTCCCTGGCACCAACGTG 3306	
		_		AAACTTCGCTATCTGAGCTCTAGAACTGCAGGGTACAAGTCACTGCAGAAGATCACCATG 3417	
	٥			AAGCTCCGTTACCTCAGCTCCAGAACAGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3366 ACCCAGTCCACAGTGCCCCTGAACCTCATTAGGGTTCACCTGATGGTGGCTGTCGAGGGG 3477	
] ]	U	-		ACCCAGTCCACAGTGCCCTGAACCTCATTAGGGTTCACGTGATGGTTGCGTGGAGGGGGGGG	
# # # # # # # # # # # # # # # # # # #				CATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC 3537	
3 D	5	~			
ij Lj				AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTC	
<b>1</b> 4	0	SBJCT:	3487		
one, duck		QUERY:	3598	TTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAG 3657	
STATES OF THE ST	ے ا	SBJCT:	3547		
] 4 =	15	QUERY:	3658	GGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTC 3717	
		SBJCT:	3607		
5	50	QUERY:	3718	AATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAAACCAGTTCCTGACCCAGCAG 3777	
		SBJCT:	3667	AATGTGAAAAGCGGAATACTACTCAAAGGCACAGGGGGAGAACCAGTTCCTGACCCAGCAG 3726	
4	55	QUERY:	3778	CCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCCGGAGCATTTCCTGTCCCAGC 3837	
	, 0	SBJCT:	3727	CCCGCCATCATCACCAGCATCATGGGTAACGGTCGCCGCAGAAGCATCTCCTGTCCCAGC 3786	
		QUERY:	3838	TGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATC 3897	
6	50			TGCAATGGCCTTGCTGAAGGCAACAAACTGTTGGCCCCCGTGGCCCTGGCTGTGGGGATC 3846	
		_		GATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGACGCATCTTTCCCTCTCGAAAT 3957	
6	65			GATGGGAGCCTCTTTGTCGGTGACTTCAATTATATCCGGCGCATCTTCCCCTTCTCGAAAC 3906	
				GTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC 4017	
	70			GTGACCAGTATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAGCCCAGGACAC 3966	
· .	70	OUERY:	4018	AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGC 4077	

	SBJCT:		
	QUERY:	078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAGACCTGGCTGG	
3	SBJCT:		
	QUERY:	138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGA 4197	
10	SBJCT:	087 GTTGTGGCCGGGACTGGCGAACAATGTCTACCCTTTGATGAAGCCCGCTGTGGGGATGGC 4146	
	QUERY:		
15	SBJCT:	147 GGGAAGGCTGTGGATGCCACCCTGATGAGCCCTAGAGGTATTGCAGTAGACAAGAACGGG 4206	
13	QUERY:		
	SBJCT:	207 CTTATGTATTTTGTTGATGCCACCATGATCCGGAAGGTCGACCAAAATGGAATCATCTCC 4266	
20	QUERY:	318 ACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATG 4377	
	SBJCT:	267 ACCCTGCTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTACCTCTAGCATG 4326	
25	QUERY:		
23	SBJCT:	GACGTGGCCCAGGTCCGTCTAGAATGGCCGACAGACCTTGCGGTCAACCCCATGGACAAT 4386	
	QUERY:	438 TCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC 4497	
30	SBJCT:	1387 TCCCTGTACGTCCTGGAGAACAACGTCATCCTGCGGATCACCGAGAATCACCAGGTCAGC 4446	
	QUERY:	1498 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTC	
35		447 ATCATCGCGGGACGGCCCATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAG 4506	
		4507 CTCGCCATCCACTCTGCTCTGGAGTCAGCCAGCGCCATCGCCATTTCTCACACCGGGGTG 4566	
40			
45			
50	-		
50			
55			
60		-	
00			
65			
70			
	5 10 15 20 25 30 35 40 45 50 55	5 QUERY: 4 SBJCT: 4 QUERY: 4 QUERY: 4 QUERY: 4 QUERY: 4 SBJCT: 4 QUERY: 4 SBJCT: 4 QUERY: 4 SBJCT: 4 QUERY: 4 SBJCT: 4 S	SBJCT: 4027 GGCGGGATCTACCGAGTCACACTCACAGCGSAGCCAAAAACACTGGCTGGAATTCGGAA 4086  QUERY: 4138 GTTGTGGCGGGACTGGCGAACTGCTTTACCCTTTGATGAAAGCCGGCTGGGAATTGGAA 4197

	5	QUERT:	5090	
		SBJCT:	5047	CACCTGCTCATGCCTGATAATCAGATCATCACCCTTACGGTGGGCACCAACGGAGGCCTC 5106
		QUERY:	5158	AAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG 5217
		SBJCT:	5107	AAAGCCGTGTCAACGCAGAACCTGGAGCTGGGCCTCATGACTTATGATGGGAACACTGGA 5166
	10			CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAA 5277
		_		
				CTCCTAGCCACCAAGAGCGATGAAACCGGATGGACAACTTTTTATGACTATGACCACGAG 5226
	15			GGCCGCCTGACCAACGTGACGCGCCCCACGGGGGTGGTAACCAGTCTGCACCGGGAAATG 5337
				GGCCGTCTGACCAATGTGACTCGCCCCACGGGGGTGGTGACCAGCCTGCACCGGGAAATG 5286
	20			GAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTGATGATGACGTCACTGTCATC 5397
				GAGAAATCCATCACCGTTGACATTGAGAACTCCAACCGTGATAACGATGTCACTGTGATT 5346
		QUERY:	5398	ACCAACCTCTCTCAGTAGAGGCCTCCTACACAGTGGTACAAGATCAAGTTCGGAACAGC 5457
	25	SBJCT:	5347	ACCAACCTCTCTTCAGTGGAGGCCTCCTACACCGTGGTACAAGATCAAGTGCGGAACAGC 5406
		OHERY.	5458	TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGC 5517
14. 3 4. 8 11. 8 11. 8	30			
1	30			TTCCACAGCGAGCCCCATGTCCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAAC 5577
Hall Hall		-		
i i	35			ATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGTGGCGCCTAAGAAAGGAACAG 5637
Man Ser				ATCTCCCTGCCCATGGAGAACGGCCTGAACTCCATCGAGTGGCGCCTGAGGAAGGA
\$ 2005 5 2005	40			ATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG 5697
	40	~		ATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCACGGAAGCACCTCCTG 5646
Hone Hones				TCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTC 5757
#	45			TCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTC 5737
	50			ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCCTTCCTCTGGCTGCCCAGCAGCGGG 5817
	50			ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCCTTCCTGTGGCTCCCCAGCAGTGGA 5766
				CTGGCAGCTGTCAACGTGTCATACTTCTTCAATGGGCGCCTGGCTGG
	55			CTGGCGGCCGTCAATGTCTCCTACTTCTTCAACGGGCGCCTGGCCGGCC
				GCCATGAGCGAGAGGACAGCATCGACAAGCAAGGCCGCATCGTGTCCCGCATGTTCGCT 5937
				GCCATGAGCGAGAGGACAGTTGACAAGCAAGGCCGGATTGTGTCCCGAATGTTCGCC 5886
	60	-		GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCCTCCTGCTTCAGAGC 5997
				GACGGGAAAGTCTGGAGCTATTCCTACCTTGACAAGTCCATGGTCCTCCTGCTGCAGAGC 5946
	65	QUERY:	5998	CAACGTCAGTATATTTTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTCACCATGCCC 6057
		SBJCT:	5947	CAGCGTCAGTACATATTTGAATATGACTCCTCTGACCGCCTCCACGCAGTCACCATGCCC 6006
		QUERY:	6058	AGCGTGGCCCGGCACAGCATGTCCACACACCCTCCATCGGCTACATCCGTAATATTTAC 6117
	70	SBJCT:	6007	AGTGTCGCCCGGCACAGCATGTCCACGCACACCTCCATTGGCTACATCCGGAACATTTAC 6066

	5	QUERY:	6118	AACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG	6177
		SBJCT:	6067	AACCCACCGGAAAGCAACGCCTCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG	6126
		QUERY:	6178	AAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAG	6237
				AAGACGTCTTTCCTGGGCACCGGGCGCCAGGTGTTCTATAAGTACGGAAAACTGTCCAAG	
		-		TTATCAGAGATTGTCTACGACAGTACCGCCGTCACCTTCGGGTATGACGAGACCACTGGT	
				TTATCGGAGATCGTCTACGACAGCACTGCCGTCACCTTCGGCTATGACGAGACCACTGGC	
	15			GTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCTGCACCATCAGGTACCGGAAG	
				GTCCTGAAGATGGTGAATCTCCAAAGCGGGGGCTTCTCCTGTACCATCAGGTACCGAAAG	
	20			ATTGGCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC	
	20			AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATA	
		=		AGGTTIGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATCATGACAACACTACCACGACAACAGCTTCCGCATCGCCAGCATCAAGCCCGTCATC	
	25			AGTGAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAA	
### ### ###	30			CACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACCAGATCATCACCACTGCCGTG	
THE STATE OF					
	35	QUERY:	6598	ATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG	6657
		SBJCT:	6547		6606
STATE SECTION	40	QUERY:	6658	TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAG	6717
Lai		SBJCT:	6607	TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGTATGGGCAGGGTCATCAAG	6666
mar dina		QUERY:	6718	AGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGG	6777
Mark Mark	45	SBJCT:	6667	AGGGAACTGAAACTGGGGCCCTATGCCAACACCCACAAAGTACACCTATGACTACGACGGG	6726
Name of the last		QUERY:	6778	GACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGACCTGGCGCTACAGCTATGAC	6837
				GACGGCCAGCTCCAGAGTGTGGCCGTCAATGACCGGCCTACCTGGCGTTATAGCTATGAC	
	50	_		CTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGCGCCTCATGCCCTTGCGC	
				CTCAATGGGAACCTGCTAAACCCAGGAAACAGTGCTCGCCTCATGCCGTTACGC	
	55			TATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGAT	
				TATGACCTCCGTGACCGGATAACCAGGCTAGGGGACGTGCAGTACAAAATCGATGATGAT GGCTATCTGTGCCAGAGAGGGTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACA	
	60			GGCTATCTGTGCCAGAGAGGGTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACA	
	00			AGAGCCTACAACAAGGCCAGCGGGTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGG	
				AGAGCGTACAACAAGGCCAGCGGGTGGAGTGTGCAGTACCGCTATGATGGCGTGAGCCGC	
	65				
		-		CGGGCTTCCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC	
	70	SBJCT:	7027	CGGGCTTCCTACAAGACCAACCTGGGCCACCACCTACAGTACTTCTATTCCGACCTCCAC	7086

		QUERY:	7138	AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTAC 7197
		SBJCT:	7087	CACCCCACACGTATCACCCATGTTTACAACCACTCCAACTCTGAGATCACCTCACTCTAC 7146
				TACGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTT 7257
				TATGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGTAGTGGGGAAGAGTACTATGTT 7206
	10			GCCTCTGATAACACAGGGACTCCTCTGGCTGTTTCAGCATCAACGGCCTCATGATCAAA 7317
				GCCTCAGATAACACCGGGACTCCTCTGGCTGTTTTTAGTATCAATGGCCTCATGATCAAG 7266
				CAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATG 7377
	15			CAACTCCAATACACAGCCTATGGGGAGATTTACTATGACTCCAATCCAGACTTTCAGATG 7326 GTCATTGGCTTCCATGGGGGACTCTATGACCCCCTGACCAAGCTGGTCCACTTCACTCAG 7437
				GTCATTGGCTTCCATGGGGGACTCTATGACCCCCTGACCAAGCTGGTCCACTCACT
	20			CGTGATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAAC 7497
	25			GTGGGCAAGGAGCCGGCCCCTTTAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGC 7557
		SBJCT:	7447	
<b>1</b> .3	20	QUERY:	7558	AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGA 7617
u	30	SBJCT:	7507	
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		QUERY:	7618	TTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCT 7677
	35	SBJCT:	7567	TTTCAGCTCAGCAACATCATTCCTGGATTCCCAAGAGCCAAAATGTATTTTGTGCCTCCC 7626
And And	40	QUERY:	7678	CCCTATGAATTGTCAGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAA 7737
#				CCCTATGAACTGTCAGAGAGCCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAG 7686
The House				CAGACAACAGAGAGACATAACCAGGCCTTCATGGCTCTGGAAGGACAGGTCATTACTAAA 7797
1000	4.5			CAGACAACAGAGGCATAACCAGGCCTTTCTGGCTCTAGAAGGACAGGTCATCTCTAAA 7746
10	45			AAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACCACCCATC 7857
				AAGCTCCATGCAGGCATCCGAGAGAAAGCAGGCCACTGGTTTGCTACGACCACGCCCATC 7806  ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGC 7917
	50			ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGCGTGTCTAGC 7866
				ATCGCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACCTGGAC 7977
	55	SBJCT:	7867	
		QUERY:	7978	AAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACTTTGTGAAGATTGGCTCAGCC 8037
	60	SBJCT:	7927	
	60	QUERY:	8038	GATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGGTG 8097
		SBJCT:	7987	
	65	QUERY:	8098	AACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTCACGAAC 8157
		SBJCT:	8047	AACGTGACCGTGTCACAGCCCACGCTGCTGGTGAACGGCAGGACTCGAAGGTTCACCAAC 8106
	70	QUERY:	8158	ATTGAGTTCCAGTACTCCACGCTGCTCCTCAGCATCCGCTATGGCCTCACCCCCGACACC 8217

		SBJCT:	8107	ATTGAATTCCAGTACTCCACGCTGCTCAGCATACGCTACGGCCTCACCCCCGACACA	0100
	5	~		CTGGACGAAGAGAAGGCCCGCGTCCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCC	
				TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGAGAGAGAG	
1					
1	10	QUERY:	8338	GGCGAGAAGCAGCACTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGGGATATTACGTG	8397
		SBJCT:	8287		8346
- 1	15	QUERY:	8398	CTTCCCGTGGAGCAATACCCAGAGCTTGCAGACAGTAGCAGCAACATCCAGTTTTTAAGA	8457
		SBJCT:	8347	CTTCCGGTGGAACAGTACCCAGAGCTGGCAGACAGTAGCAGCAACATCCAGTTCTTAAGA	8406
2	20	QUERY:	8458	CAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGCCATTCCTTGTCTGAATGGCT	8517
_	-0	SBJCT:	8407	CAGAATGAGATGGGAAAGAGGTAACAAAATAACCTGCTGCCACCTCTTCTCTGGGTGGCT	8466
				CAGCAGGAGTAACTGTTATCTCCTCTCCTAAGGAGATGAAGACCTAACAGGGGCACTGCG	
2	25			CAGCAGGAGCAACTGTGACCTCCTCTCCTAAGGAGACCAAGACCTAACAGGGGCACTGAG	
***** *****				GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT	
£1.	30			GCCGGGCTGCTTTAGGACCCCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT	
100 0 000 100 0 000 100 0 000				ACTGTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGGCTGAAAATTCCGA	
	25			ACTGTCCAAGCGCAAAGTCCCTCATCCTGAAGTAGACTAGAGCTCGGCCACAAATTCTGA	0040
W	33			GGAAACAAAC 8709           GGAAACAAAC 8658	
And Spins spins a grap in it is not not not a last, hard from Spins a last.	40	SCORE :	= 145 ITIES	9 BITS (736), EXPECT = 0.0 = 1081/1196 (90%) LUS / PLUS	
		QUERY:	270	ATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGGACGCTGTGG	329
	45	SBJCT:	123	ATCTGCAATAATGGATGTGAAGGATCGGCGACATCGCTCTTTGACCAGGGGACGGTGTGG	182
•		QUERY:	330	CAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACA	
	50	SBJCT:	183	CAAGGAGTGTCGCTACACCAGCTCCTCTCTGGACAGTGAGGACTGCCGTGTGCCCACGCA	
		QUERY:	390	GAAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTA	
	<i></i>	SBJCT:		GAAGTCCTACAGTTCCAGTGAGACCCTGAAGGCTTATGACCATGACAGCAGAATGCACTA	
	55	QUERY:	450	TGGAAACCGAGTCACAGACCTCATCCACCGGGAGTCAGATGAGTTTCCTAGACAAGGAAC	
			202		
		SBJCT:		TGGAAACCGAGTCACAGACCTGGTGCACCGGGAGTCCGATGAGTTTTCTAGACAAGGGGC	
	60	QUERY:	510	CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG	569
	60	QUERY:	510 363	CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG	569 422
		QUERY:	510 363 570	CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG	569 422 629
	60 65	QUERY: SBJCT: QUERY:	510 363 570 423	CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG	<ul><li>569</li><li>422</li><li>629</li><li>482</li></ul>
		QUERY: SBJCT: QUERY: SBJCT:	<ul><li>510</li><li>363</li><li>570</li><li>423</li><li>630</li></ul>	CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG	<ul><li>569</li><li>422</li><li>629</li><li>482</li><li>689</li></ul>

	QUERY: 690 ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAAACTCGGCCCTTACCCTGACTGA
5	QUERY: 750 TGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTACATCCTCGCC 809
10	QUERY: 810 TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 869
1.7	QUERY: 870 GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGA 929
15	SBJCT: 723 GATGCCATTGCTAGACAGCAACACCTCCCATCAGATCATGGACACCCCGATGAGGA 782  QUERY: 930 ATTCTCCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989
20	SBJCT: 783 ATTCTCCCCTAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGTAG 842  QUERY: 990 TGGCCCTCCGAACCACCACGAGCCAGTCGACTCTGAGGCCCCCTCTCCCACCCCCCTCACAA 1049
25	QUERY: 1050 CCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109
[] [] 30	QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACACA
Post Post	QUERY: 1170 GTCCGTTCAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCA 1229
1 35 1 35	SBJCT: 1023 GTCCGTTCAGCTCCAGGACAGCTGGGTGCTGAACAGTAACGTGCCGCTGGAGACGCGGCA 1082
2. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.	QUERY: 1230 CTTCCTCTTCAAGACCTCCTCGGGGAGCACCCCTTGTTCAGCAGCTCTTCCCCCGGGATA 1289
40	SBJCT: 1083 CTTCCTCTTCAAGACGTCCTCCGGAAGCACCCCTGTTCAGCAGCTCTTCTCCAGGATA 1142
Anna Santa Buran B	QUERY: 1290 CCCTTTGACCTCAGGAACGGTTTACACGCCCCGCCCGCCTGCTGCCCAGGAATACTTT 1349
45	QUERY: 1350 CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGC 1409
50	QUERY: 1410 CCTCTCCGCCATTGCCGCGGCCCTCCTCTTGGCTATTTTGCTGGCGTATTTCATAG 1465
55	SCORE = 1427 BITS (720), EXPECT = 0.0 IDENTITIES = 996/1088 (91%) STRAND = PLUS / PLUS
60	QUERY: 1464 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523
00	QUERY: 1524 GGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAG
65	QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAG 1643
70	QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGAAGGA 1703

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SBJCT: 1620 AAGAGGACTGCCACCATCTCATGCACAGTATGACTTCATGGAACGCCTGGACGGAAAGGA 1679
     QUERY: 1704 GAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAA 1763
              SBJCT: 1680 GAAGTGGAGTGTGGTCGAGTCACCCAGGGAACGCCGGAGCATCCAGACCCTGGTGCAGAA 1739
  5
     QUERY: 1764 TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823
              SBJCT: 1740 CGAGGCTGTGTTCGTGCAGTACTTGGATGTGGGCCTGTGGCACCTCGCCTTCTACAATGA 1799
 10
     QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTG 1883
              SBJCT: 1800 CGGCAAGGACAAGGAGTGTCTCCTTCAATACGGTTGTCTTAGATTCAGTGCAGGACTG 1859
     QUERY: 1884 TCCACGTAACTGCCATGGGAATGGTGAATGTGTCCCGGGGTGTGTCACTGTTTCCCAGG 1943
 15
              TCCACGAAACTGCCACGGGAACGGCGAATGCGTGTCTGGACTGTTCACTGTTTCCCAGG 1919
     20
              SBJCT: 1920 ATTCCTAGGTGCAGACTGCGCTAAAGCTGCCTGTTCTGTGCAGTGGGAATGGACA 1979
     QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCC 2063
              SBJCT: 1980 GTATTCCAAAGGGACATGCCAGTGCTACAGTGGCTGGAAAGGAGCAGAATGCGATGTGCC 2039
 25
     QUERY: 2064 CATGAATCAGTGCATCGATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2123
              SBJCT: 2040 CATGAACCAGTGCATCGATCCTTCCTGTGGGGGCCCACGGCTCCTGCATTGATGGGAACTG 2099
JI 30
     QUERY: 2124 TGTCTGCTGCTGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCCAC 2183
Ĭij.
              Ľ.
     SBJCT: 2100 CGTGTGTGCAGCTGGCTACAAGGGCGAGCACTGCGAAGAAGTGGATTGCTTGGATCCAAC 2159
r.,
      1 35
              11
      SBJCT: 2160 CTGCTCCAGCCATGGTGTCTGTGTAACGGAGAGTGTCTATGCAGCCCCGGCTGGGGCGG 2219
Ti.
      QUERY: 2244 TCTGAACTGTGAGCTGCGAGGGTCCAGTGCCAGACCAGTGCAGTGGCATGGCACGTA 2303
              40
      SBJCT: 2220 GCTCAACTGCGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGTAGTGGGCATGGCACTTA 2279
Tu.
Tank
Tank
      QUERY: 2304 CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363
Bra.
              100 A
      SBJCT: 2280 CCTCCCTGACTCTGCCACTGTGAACTGTGATCCGAATTGGATGGGTCCCGACTGCTCTGT 2339
 45
      QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2423
              SBJCT: 2340 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2399
 50
      SBJCT: 2400 TGAAGAGGGCTGGACAGGCGCGCTTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2459
      QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543
 55
              SBJCT: 2460 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2519
      QUERY: 2544 CACCATTG 2551
  60
              1111111
      SBJCT: 2520 CACCATTG 2527
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In this search it was also found that the FCTR3bcd and e nucleic acid had homology to six fragments of *Gallus gallus* partial mRNA for teneurin-2. It has 2780 of 3449 bases (80%) identical to bases 3386-6834, 1553 of 1862 bases (83%) identical to bases 1414-3275, 540 of

65

628 bases (85%) identical to bases 587-1214, 593 of 725 bases (81%) identical to bases 7084-7808, 429 of 515 bases (83%) identical to bases 7895-8409, and 397 of 475 bases (83%) identical to bases 20-494 of Gallus gallus partial mRNA for teneurin-2. (EMBL Acc: GGA278031) (Table 30).

#### Table 3O. BLASTN of FCTR3b, c, d, and e against Gallus gallus Teneurin-2 mRNA (SEQ 5 ID NO:67)

>GI 10241573 EMB AJ279031.1 GGA279031 GALLUS GALLUS PARTIAL MRNA FOR TENEURIN-2 (TEN2 GENE), LONG SPLICE VARIANT 10 LENGTH = 8409SCORE = 1532 BITS (773), EXPECT = 0.0 IDENTITIES = 2780/3449 (80%) STRAND = PLUS / PLUS 15 QUERY: 3458 TGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGG 3517 SBJCT: 3386 TGATGGTAGCAGTAGAAGGGCATCTATTTCAAAAATCATTTCTGGCATCTCCCAACTTGG 3445 QUERY: 3518 CCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAG 3577 20 SBJCT: 3446 CTTATACATTCATCTGGGACAAAACAGATGCATATGGTCAGAAGGTTTATGGGTTGTCAG 3505 1... ¥Ž QUERY: 3578 ATGCTGTTGTCTGTCGGGTTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGA 3637 Hart strike 25 SBJCT: 3506 ATGCTGTAGTTTCTGTGGGTTTTGAATATGAGACTTGTCCCAGTTTGATTCTGTGGGAGA 3565 T. QUERY: 3638 AAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCC 3697 la is 2 mg SBJCT: 3566 AAAGGACTGCGCTGCAAGGATTTGAGCTAGATCCTTCCAATCTAGGAGGATGGTCTT 3625 30 Ti, QUERY: 3698 TAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAA 3757 £.; SBJCT: 3626 TGGATAAACATCATGTACTGAATGTCAAGAGTGGTATATTGCACAAAGGCAATGGAGAAA 3685 mil II II Han. 35 QUERY: 3758 ACCAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCC 3817 SBJCT: 3686 ATCAGTTTCTAACTCAGCAGCCAGCTGTGATAACCAGCATTATGGGGAATGGGCGCCGAA 3745 40 QUERY: 3818 GGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAG 3877 SBJCT: 3746 GAAGCATATCCTGTCCTAGCTGCAATGGTCTTGCAGAAGGAAATAAGCTTTTGGCCCCTG 3805 QUERY: 3878 TGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGAC 3937 45 SBJCT: 3806 TAGCACTGGCAGTGGGAATTGATGGAAGCCTCTTTGTTGGAGATTTTAATTACATTCGGC 3865 OUERY: 3938 GCATCTTTCCCTCTGGAAATGTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAAC 3997 SBJCT: 3866 GTATCTTCCCATCCAGGAATGTGACTAGCATATTGGAGCTGAGAAATAAAGAGTTTAAAC 3925 50 SBJCT: 3926 ATAGCAACAATCCTGCTCACAAATACTATCTGGCCGTGGACCCCGTTTCGGGCTCCCTGT 3985 55 QUERY: 4058 ACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAG 4117 SBJCT: 3986 ACGTATCAGACACCAACAGCCGACGGATATACAAAGTCAAATCTCTTACTGGCACGAAAG 4045 60 QUERY: 4118 ACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATG 4177 

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		QUERY:	4178	AAGCCCGCTGCGGGGATGGAGGCAAGCCATAGATGCAACCCTGATGAGCCCGAGAGGTA 4237
		SBJCT:	4106	AAGCCAGATGTGGAGATGGAGGAAAGCAGTGGACGCAACCCTAATGAGTCCTCGAGGAA 4165
				TTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGATCCGGAAGGTTG 4297
				TTGCAGTGGATAAGTATGGACTCATGTATTTTGTTGATGCCACTATGATTCGAAAAGTGG 4225
	10			ACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGC 4357
				ATCAGAATGGAATTATATCAACTCTGCTGGGCTCCAATGACCTAACTGCCGTCCGACCTC 4285
		_		TGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCCAACAGACCTTG 4417
	15			TAAGCTGTGATTCCAGCATGGATGTCAGCCAGGTACGGCTGGAGTGGCCTACTGATCTCG 4345
				CTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCA 4477
	20			CTGTCGATCCCATGGACAACTCACTTTATGTCCTAGAGAACAATGTTATTTTACGGATCA 4405
				CCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCA 4537
				CAGAAAACCATCAAGTTAGCATTATTGCTGGACGCCCCATGCACTGCCAGGTTCCTGGTA 4465
	25			TTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTG 4597
253				TAGACTACTCTTTAGCAAACTGGCTATTCATTCCGCACTTGAATCAGCCAGTGCCATTG 4525
	30			CCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTC 4657
STATE STATE				CCATCTCACACACAGGAGTTCTTTACATCAGTGAGACAGATGAAAAAAAA
F-3	35	-		TACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCG 4717
				TACGCCAGGTAACTACCAATGGAGAAATATGCCTTCTTGCAGGGGCAGCTTCAGACTGTG 4645
****	40			ACTGCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATG 4777
				CCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCATTTACATTGCAG 4837
suf il M				
Han Hall	45			ACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCA 4897
de la				
	50	QUERY:	4898	ACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCA 4957
	30	SBJCT:	4826	
		QUERY:	4958	TCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTCACATATAGTA 5017
	55	SBJCT:	4886	TTCACCAGTACACTCTCAGCCTTGTTACCGGGGAGTACTTGTACAATTTCACCTATAGCA 4945
		QUERY:	5018	CTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCCTGAAGATCCGTCGGG 5077
	60	SBJCT:	4946	GTGATAACGATGTCACCGAGGTGATGGACAGCAATGGCAACTCCTTGAAGGTCCGTCGGG 5005
	00	QUERY:	5078	ACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCAGATCATCACCCTCACCG 5137
		SBJCT:	5006	5 ATGCCAGCGGAATGCCCCGCCATTTACTGATGCCTGATAATCAGATTGTCACGCTGGCCG 5065
	65	QUERY:	5138	TGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGA 5197
		SBJCT:	5066	5 TTGGCACTAATGGTGGACTCAAACTAGTCTCAACGCAGACCCTGGAACTTGGATTAATGA 5125
	70	QUERY:	5198	CCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTT 5257

	SBJCT:	5126	CTTATAACGGAAACAGTGGTCTCTTAGCAACGAAGAGTGATGAAACAGGATGGACAACAT	2182
	QUERY:	5318	CCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTG	5377
	SBJCT:	5246	CTAGCCTTCATCGAGAAATGGAAAAGTCTATTACCATCGACATTGAGAATTCTAATCGGG	5305
10	QUERY:	5378	ATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTAC	5437
	SBJCT:	5306	ATGATGATGTCACGGTCATCACAAATCTCTCCTCTGTGGAGGCTTCCTATACAGTTGTTC	5365
15				
			AAGATCAAGTGAGGAACAGCTACCAGCTCTGTAATAATGGTACTTTGAGAGTGATGTATG	
20				
25				
25				
30			TCCATGGAAGAATCTCTTGTCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCT	
35	QUERY:	5738	ATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCCTTCC	5797
	SBJCT:	5666	ACGATGATCACCGCAAGTTCACCCTGAGGATAATTTACGATCAGCTGGGACGGCCCTTCC	5725
40	QUERY:	5798	TCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTTCAATGGGCGCC	5857
70	SBJCT:	5726	TCTGGCTGCCCAGCAGCGGCCTGGCTGCCGTCAACGTGTCCTATTTCTTCAACGGGCGCC	5785
45			TGGCTGGGCTTCAGCGCGGAGCCATGAGCGAAAGGACATCGACAAGCAAG	
	-			
50				
55				
<i>c</i> 0	QUERY:	6098		6157
60	SBJCT:	6026		6085
	QUERY:	: 6158	GTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACA	6217
65	SBJCT:	: 6086		6145
	QUERY:	6218		6277
70	SBJCT	: 6146	AGTATGGAAAGCTATCCAAATTATCTGAAATTGTTTATGACAGTACTGCGGTTACTTTTG	6205
	5 10 15 20 25 30 35 40 45 50 66 65	QUERY:  5 SBJCT: QUERY: 10 QUERY: SBJCT: 15 QUERY: SBJCT: QUERY: QUERY: QUERY: 30 SBJCT: QUERY: SBJCT: QUERY: SBJCT: QUERY: 55 QUERY: SBJCT: QUERY: 40 SBJCT: QUERY: 50 QUERY: SBJCT: QUERY: SBJCT: QUERY: SBJCT: QUERY: SBJCT: QUERY: SBJCT: QUERY: SBJCT:	QUERY: 5258  5 SBJCT: 5186 QUERY: 5318  10 QUERY: 5378 SBJCT: 5246 QUERY: 5378 SBJCT: 5306  15 QUERY: 5438 SBJCT: 5426 QUERY: 5498 QUERY: 5498 QUERY: 5558  25 SBJCT: 5486 QUERY: 5618 30 QUERY: 5678 SBJCT: 5606 35 QUERY: 5738 SBJCT: 5666 QUERY: 5738 SBJCT: 5726 QUERY: 5798 SBJCT: 5726 QUERY: 5918  50 QUERY: 5918 SBJCT: 5906 55 QUERY: 5906 55 QUERY: 6038 SBJCT: 5906 60 SBJCT: 5966 QUERY: 6038 SBJCT: 6026 QUERY: 6158 SBJCT: 6026 QUERY: 6158 SBJCT: 6146	SBJCT: 5186 TTTATGACTATGATCATCAGAGGGGCCTGACCAATGTAACACTGCCACTGGGAATGTAAC QUERY: 5318 CAGTCTGCACCGGGAAATGGAAACTGTAACACTGAGAATCTAACACTGGACTGAGAACTGAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGAGAATGTAACACTGGTACACATGTACACATGTACACTGACACTGACACACAC

				GGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCT	
	5	QUERY:	6338	GCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCG	6397
				GTACAATCCGCTATCGTAAAATTGGCCCTCTTGTTGACAAACAA	
	10			AGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCG	
				AAGAAGGTATGGTCAATGCAAGGTTTGATTATACATATCACGACAATAGTTTTCGCATTG	
	1.5	_		CAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATG	
	15			CAAGCATCAAACCCATCATAAGTGAGACTCCTCTTCCAGTTGATCTTTACCGTTATGATG	
		-		AGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACC	
	20			AGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCA	
		SBJCT:	6506		6565
	25	QUERY:	6638	AGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACA	6697
		SBJCT:	6566		6625
Men thus	30	QUERY:	6698	GCATGGGCAGGGTGATCAAGAGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGT	6757
Ti:	30	SBJCT:	6626	GCATGGGAAGATAACTAAAAGAGAACTGAAACTTGGGCCGTATGCCAACACCAAGT	6685
		QUERY:	6758	ACACCTATGACTACGATGGGGACGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGA	6817
	35			ATACCTATGATTATGATGGAGATGGGCAATTGCAAAGCGTAGCAGTAAATGATAGGCCTA	
Ĭij.				CCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTG	
De ser re	40			CCTGGCGTTACAGTTATGACCTGAATGGAAATCTTCACCTCCTGAATCCTGGAAACAGTG	6805
THE PARTY OF THE P				TGCGCCTCATGCCCTTGCGCTATGACCTC 6906	
House made	45			41 BITS (626), EXPECT = 0.0	
den 7 den 12	73	IDENT	ITIES	= 1553/1862 (83%) LUS / PLUS	
	50			AGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCGGGTAACACAAGAAGTCCCACCA	
				AGCAGCATAGATAGTGGAGAAACAGAAGTTGGCCGCAAGGTCACCCAAGAGGTGCCCCCT	
	سر سر			GGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC	
	55			GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCCTGAAGTTCAACATA	
		-		TCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCAT	
	60			GCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGAGAGTGGAGTGTGGTTGAGTCT	
	65	QUERY:	1726	CCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTAC	1785
		SBJCT:	1654		1713
	70	QUERY:	1786	CTGGATGTGGGCCTGTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT	1845

		SBJCT:	1714	TTGGATGTGGGTTTGTGGCACCTGGCGTTTTTACAATGATGGCAAGGACAAAGAAGTGGTC 1	. / / 3
				TCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAAT 1	
				GGTGAATGTGTCCGGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCT 1	
		SBJCT:	1834	GGCGAGTGTGTTTCTGGTGTCTGCCACTGTTTTCCCGGATTTCATGGAGCAGATTGTGCT	1893
	10	QUERY:	1966	AAAGCTGCCTGTCCTGTGCAGTGGGAATGGACAATATTCTAAAGGGACGTGCCAG	2025
		SBJCT:	1894	AAAGCTGCCTGCCCGGTGCTGCAGTGCCAATGGTCAGTACTCCAAAGGAACCTGCTTG	1953
	15			TGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCCCATGAATCAGTGCATCGATCCT	
				TGCTACAGTGGCTGGAAAGGTCCGGAATGTGATGTACCCATCAGCCAGTGTATTGATCCC	
	20	-		TCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTGTGTCTGCTCTGCTGCTACAAA 2	
				TCGTGTGGAGGTCATGGTTCCTGCATCGAAGGGAACTGTGTCTGTTCCATTGGCTATAAA	
	25			GGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGT :	
	23			GTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGGTCTGAACTGTGAGCTGGCGAGG	
¥.,					
free New	30			GTCCAGTGCCAGACCAGTGCAGTGGGCATGCCACGTACCTGCCTG	
Hart Hart		SBJCT:	2194		2253
i si	35	QUERY:	2326	AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGT	2385
Built Hall		SBJCT:	2254	AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCCGTTGAAGTGTGCTCTGTAGACTGT	2313
# # # # # # # # # # # # # # # # # # #	40	-		GGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCA	
may aver.				GGCACCCATGGGGTGTGCATTGGCGGAGCGTGTCGCTGTGAAGAAGGGTGGACAGGAGTG	
1000	4.5			GCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGAGCACGGGACCTGTAAAGATGGC	
Man Ama	45			GCGTGTGACCAGCGTGTGTCATCCCCGGTGTACAGAGCACGGAACTTGTAAAGATGGG  AAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAACGGCA	
				AAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAACGGCACAATGGTGAATGTGAATGCAGAGAGAG	
	50			GGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGT	
	55	QUERY:	2626	CAGAACAGCTGGCAGTGTCTCCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCC	2685
		SBJCT:	2554	CAGAACAGCTGGCAGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCC	2613
	60	QUERY:	2686	ATGGAAACTTCCTGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTG	2745
	00	SBJCT:	2614		2673
		QUERY:	2746	GACCCTGACTGCCTGCAGTCAGCCTGTCAGAACAGCCTGCTCTGCCGGGGGTCCCCGG	2805
	65			GTCCCAGATTGCTGCCTCCAGTCCACTTGTCAAAACAGCCTGCTGTGCCGGGGTTCCCGC	
				GACCCACTGGACATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTAT	
	70	SBJCT:	2734	GATCCTCTTGACATCATACAACAGAGCCATTCTGGTTCACCAGCTGTGAAGTCATTCTAT	2793

	QUERY: 2866 GACCGTATCAAGCTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCT 2925
5	QUERY: 2926 TTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCAAGTAGTAACTACAGATGGAACTCCC 2985
10	QUERY: 2986 CTGGTCGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGC 3045
15	QUERY: 3046 CAGGATGGCACGTTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAG 3105
20	QUERY: 3106 CGAGCCCCGTTCATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCC 3165
	QUERY: 3166 ATGGACACCCTGGTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGC 3225
25	QUERY: 3226 TTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCC 3285
30 and 500 and	QUERY: 3286 CCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCT 3345
14 35 11	QUERY: 3346 GG 3347    SBJCT: 3274 GG 3275
# 40	SCORE = 547 BITS (276), EXPECT = E-152 IDENTITIES = 540/628 (85%) STRAND = PLUS / PLUS
45	QUERY: 782 GTCGTCCCATTCCACCTACATCCTCGCCTAGTCTCCCCATCTGCTCAGCTGCCTAGCT 841
<b>Š</b> nik <b>50</b>	QUERY: 842 CCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCATC 901
30	QUERY: 902 AAATCATGGACACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCAT 961
55	SBJCT: 767 GTTCAGGGCCACAGCAGCAGCAGCAGCAGCACCACCACCACCA
60	SBJCT: 827 TGAGGCCACCTCTCCCCCCCTCCTCACAACCACTCGCTGTCCCATCATCACTCGTCTGCCA 886  OUERY: 1082 ACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCAG 1141
65	SBJCT: 887 ACTCCCTCAACAGGAACTCGCTCACCAACCGCGCGCAACCAGATCCACGCGCCTGCTCCCG 946  QUERY: 1142 CGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGGACAGCTGGGTGCTAA 1201
70	SBJCT: 947 CTCCCAATGACCTGGCGACCACGCCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTCA 1006  QUERY: 1202 ACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACAC 1261

	5	QUERY: 1262 CCTTGTTCAGCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCC 1321
	5	SBJCT: 1067 CGCTGTTCAGTAGCTCTTCCCCTGGCTACCCACTGACCTCAGGAACAGTTTATACTCCAC 1126
		QUERY: 1322 CGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCT 1381
	10	SBJCT: 1127 CTCCCAGGCTGTTACCTAGAAATACATTTTCCAGGAATGCATTCAAGCTGAAAAAGCCCT 1186
		QUERY: 1382 CCAAATACTGCAGCTGGAAATGTGCTGC 1409
	15	SBJCT: 1187 CCAAGTATTGTAGCTGGAAATGTGCTGC 1214
		SCORE = 391 BITS (197), EXPECT = E-105 IDENTITIES = 593/725 (81%) STRAND = PLUS / PLUS
	20	QUERY: 7156 CATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCAC 7215
		SBJCT: 7084 CATGTCTACAATCATTCCAATTCAGAAATTACCTCTCTGTATTATGATCTGCAAGGCCAC 7143
	25	QUERY: 7216 CTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGG 7275
		SBJCT: 7144 CTCTTTGCAATGGAGAGTAGCAGTGGGGAAGAATATTATGTCGCCTCCGATAACACGGGC 7203
######################################	30	QUERY: 7276 ACTCCTCTGGCTGTGTTCAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCC 7335
Įij.	30	QUERY: 7336 TATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGG 7395
9 15 1	35	SBJCT: 7264 TACGGAGAGATTTATTATGACTCAAACCCTGATTTCCAGCTGGTTATTGGGTTCCATGGA 7323
1[]		QUERY: 7396 GGACTCTATGACCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTG 7455
#		SBJCT: 7324 GGGCTGTATGATCCTTTAACCAAACTCGTCCATTTTACCCAAAGGGACTACGATGTCCTT 7383
Hand made three	40	QUERY: 7456 GCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCC 7515
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		SBJCT: 7384 GCTGGACGCTGGACATCTCCTGATTACACAATGTGGAAAAACATTGGTAGAGAACCTGCT 7443
The House	45	QUERY: 7516 CCCTTTAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAG 7575
insk		SBJCT: 7444 CCCTTCAATCTGTACATGTTCAAGAGTAACAACCCTCTCAGCAATGAACTGGATCTAAAG 7503
	<b></b>	QUERY: 7576 AACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTCAGCTTAGCAACATC 7635
	50	SBJCT: 7504 AATTATGTAACAGATGTCAAAAGCTGGCTGGTGATGTTCGGATTTCAGCTTAGCAACATT 7563  QUERY: 7636 ATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCCTATGAATTGTCAGAG 7695
		QUERY: 7636 ATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCCTATGAATTGTCAGAG 7633
	55	QUERY: 7696 AGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACAT 7755
		SBJCT: 7624 AGTCAAGCGTGTGAAAATGGACAGCTAATTACAGGAGTCCAGCAGACAACAGAAAGACAC 7683
	60	QUERY: 7756 AACCAGGCCTTCATGGCTCTGGAAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATC 7815
		SBJCT: 7684 AATCAAGCTTTCATGGCTCTTGAGGGACAGGTCATATCTAAAAGATTACATGCCAGTATT 7743
	65	QUERY: 7816 CGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACCACCATCATTGGCAAAGGCATCATG 7875
	UJ	
		QUERY: 7876 TTTGC 7880
	70	SBJCT: 7804 TTTGC 7808

15966-697

SCORE = 339 BITS (171), EXPECT = 2E-89 IDENTITIES = 429/515 (83%) STRAND = PLUS / PLUS 5 OUERY: 7967 ACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACTTTGTGAAGA 8026 SBJCT: 7895 ACTACCTGGAAAAAATGCACTACAGCATCGAGGGGAAGGATACTCACTACTTTGTCAAGA 7954 QUERY: 8027 TTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCATCGGCCGCAAGGTGCTAG 8086 10 SBJCT: 7955 TAGGCTCAGCCGATAGCGACCTCGTCACCCTCGCGATGACCAGCGGGAGGAAGGTCCTGG 8014 QUERY: 8087 AGAGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAA 8146 15 SBJCT: 8015 ACAGCGGAGTAAACGTGACCGTCTCCCAGCCAACCCTCCTTATCAACGGAAGGACTCGAC 8074 QUERY: 8147 GGTTCACGAACATTGAGTTCCAGTACTCCACGCTGCTCAGCATCCGCTATGGCCTCA 8206 SBJCT: 8075 GGTTCACAAACATCGAGTTTCAGTATTCCACCCTGCTGATCAACATCCGCTACGGGCTCA 8134 20 QUERY: 8207 CCCCCGACACCCTGGACGAAGAGAGAGGCCCGCGTCCTGGACCAGGCGAGACAGAGGCCC 8266 SBJCT: 8135 CCGCCGACACGCTGGATGAGGAGAAGGCACGAGTGCTAGACCAGGCTCGGCAGCCGAGCCC 8194 25 SBJCT: 8195 TGGGGTCGGCCTGGGCCAAAGAGCAGCAGAAGGCACGGGATGGCCGCGAGGGCAGCCGCG 8254 ₩ 30 QUERY: 8327 TGTGGACTGAGGGCGAGAAGCAGCTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGG 8386 M SBJCT: 8255 TATGGACAGACGAGAGAGAGCAACAGCTTCTGAACACGGGAAGGGTTCAAGGTTACGAGG 8314 100 581 585 QUERY: 8387 GATATTACGTGCTTCCCGTGGAGCAATACCCAGAGCTTGCAGACAGTAGCAGCAACATCC 8446 **35** SBJCT: 8315 GATATTATGTCTTGCCTGTGGAGCAGTACCCAGAGCTAGCAGACAGTAGCAGCAACATCC 8374 ĮĮ. M OUERY: 8447 AGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAA 8481 **40** SBJCT: 8375 AGTTTTTAAGACAGAATGAAATGGGAAAGAGGTAA 8409 SCORE = 323 BITS (163), EXPECT = 1E-84 ---IDENTITIES = 397/475 (83%) Lin STRAND = PLUS / PLUS C 45 QUERY: 299 GACACCGCTCTTTGACCAGAGGACGCTGTGGCAAAGAGTGTCGCTACACAAGCTCCTCTC 358 ļ. GACACCGCTCTTTGACGAGAGGCCGGTGCGGGAAGGAGTGTCGCTATACTAGTTCTTCAC 79 SBJCT: 20 QUERY: 359 TGGACAGTGAGGACTGCCGGGTGCCCACACAGAAATCCTACAGCTCCAGTGAGACTCTGA 418 50 SBJCT: 80 QUERY: 419 AGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACC 478 55 SBJCT: 140 AAGCATATGGCCATGACACGAGGATGCACTACGGAAATCGAGTTTCAGACCTGGTTCACA 199 QUERY: 479 GGGAGTCAGATGAGTTTCCTAGACAAGGAACCAACTTCACCCTTGCCGAACTGGGCATCT 538 SBJCT: 200 GGGAGTCGGATGAGTTTCCAAGGCAAGGAACGAACTTCACCCTTGCAGAACTGGGAATCT 259 60 QUERY: 539 GTGAGCCCTCCCCACACCGAAGCGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCT 598 SBJCT: 260 GTGAGCCCTCTCCCCATCGAAGTGGCTACTGCTCGGACATAGGAATACTCCATCAAGGCT 319 65 SBJCT: 320 ATTCCTTGAGCACTGGCTCTGATGCTGACTCAGACACGGAGGGCGGGATGTCTCCAGAGC 379 OUERY: 659 ACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTC 718 70

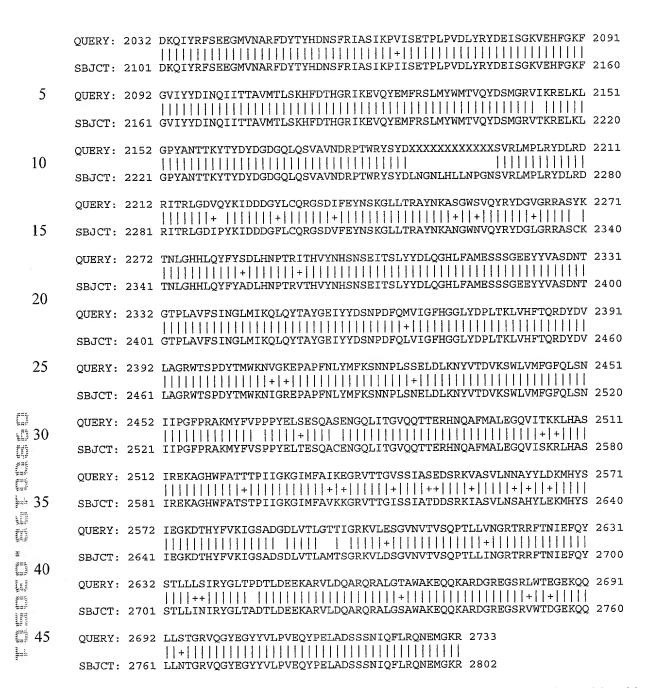
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SBJCT: 380 ACGCGATCAGGCTGTGGGGAAGAGGGATCAAATCCAGCCGAAGTTCTGGCCTGTCAAGTC 439
             QUERY: 719 GTGAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGA 773
      5
                               SBJCT: 440 GTGAAAACTCGGCTCTCACGCTCACTGACTCCGACAATGAGAACAAGTCAGATGA 494
                        The full FCTR3a amino acid sequence also has 342 of 383 amino acid residues (89%)
             identical to, and 342 of 383 residues (89%) positive with, the 276 amino acid residue Odd
             Oz/ten-m homolog 2 (Drosophila) (GenBank Acc: NP 035986.2) (SEQ ID NO:68) (Table 3P).
    10
                    Table 3P. BLASTP of FCTR3a against Odd Oz/ten-m homolog 2 - (SEQ ID NO:68)
              >GI | 7657415 | REF | NP 035986.2 | ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M HOMOLOG
                                (DROSOPHILA) [MUS MUSCULUS]
    15
               GI 4760778 DBJ BAA77397.1 (AB025411) TEN-M2 [MUS MUSCULUS]
                              LENGTH = 2764
               SCORE = 495 BITS (1274), EXPECT = E-139
               IDENTITIES = 342/383 (89%), POSITIVES = 342/383 (89%), GAPS = 41/383 (10%)
    20
                               HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 96
                                SBJCT: 189 HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 248
The seasons
                               RPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 156
    25
              QUERY: 97
                                State of the state
              SBJCT: 249 RPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 308
              OUERY: 157 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPS 216
Li
    30
                                H
              SBJCT: 309 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPS 368
111
              QUERY: 217 KYCSWKCAALSAIAAALLLAILLAYFI------ 243
Butte work street speed
                                SBJCT: 369 KYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRTGLPGNDDV 428
     35
              QUERY: 244 ------VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 295
                                             SBJCT: 429 ATVPSGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 488
     40
               QUERY: 296 ALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGL 355
                                SBJCT: 489 ALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGL 548
     45
               OUERY: 356 WHLAFYNDGKDKEMVSFNTVVLD 378
                                SBJCT: 549 WHLAFYNDGKDKEMVSFNTVVLD 571
                         The full FCTR3b amino acid sequence has 2442 of 2802 amino acid residues (87%)
               identical to, and 2532 of 2802 residues (90%) positive with, the 2802 amino acid residue
     50
               teneurin-2 [Gallus gallus] (GenBank Acc: AJ279031) (SEQ ID NO:69) (Table 3Q).
                                Table 3Q. BLASTP of FCTR3a against Teneurin-2 - (SEQ ID NO:69
               >GI | 10241574 | EMB | CAC09416.1 | (AJ279031) TENEURIN-2 [GALLUS GALLUS]
                               LENGTH = 2802
     55
                SCORE = 4853 BITS (12589), EXPECT = 0.0
                 IDENTITIES = 2510/2802 (87%), POSITIVES = 2600/2802 (90%), GAPS = 69/2802 (2%)
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		QUERY:	1	MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 6	0
		SBJCT:	1	MDIKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPAQKSYSSSETLKAYGHDTRMHYGNR 6	0
	5	QUERY:	61	VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 1:  +  +	
		SBJCT:	61	VSDLVHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDIGILHQGYSLSTGSDADSDTE 1	
	10	QUERY:	121	GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDENG 1	
		SBJCT:	121	GGMSPEHAIRLWGRGIKSSRSSGLSSRENSALTLTDSDNENKSDEENDFHTHLSEKLKDR 1	
		QUERY:	169	RPIPPTSSPSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDT 2	
	15	SBJCT:		QTSWQQLAETKNSLIRRPIPPTSSSSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDT 2	
		QUERY:		NPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNHTLSHHHSSANSLNR 2	
	20	SBJCT:		NPDEEFSPNSYLLRACSGPQQASSSGPSNHHSQSTLRPPLPPPHNHSLSHHHSSANSLNR 3	
		QUERY:		XXXXXXXQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXX 3	
	25	SBJCT:		XXXXYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPSKYCSWKCXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	
	23	SBJCT:			
14 14 14 14 14 14 14 14 14 14 14 14 14 1		QUERY:		YFIVPWSLKNSSIDSGEAE 4	
ŢĮ.	30	SBJCT:			
Strate affects through	35	QUERY:	412	VGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERL 4	471
ļ.		SBJCT:	481	+	540
		QUERY:	472	DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDS	531
\$	40	SBJCT:	541	DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKDKEVVSFSTVILDS	600
Hart Ham the	70	QUERY:	532	VQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCQCYSGWKGAE 5	591
		SBJCT:	601	VQDCPRNCHGNGECVSGVCHCFPGFHGADCAKAACPVLCSGNGQYSKGTCLCYSGWKGPE (	
	45	QUERY:	592	CDVPMNQCIDPSCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSP (	
₹***		SBJCT:	661	CDVPISQCIDPSCGGHGSCIEGNCVCSIGYKGENCEEVDCLDPTCSNHGVCVNGECLCSP	
	50	QUERY:			
		SBJCT:		GWGGINCELPRAQCPDQCSGHGTYLSDTGLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGG	
	55	QUERY:			
	33	SBJCT:			
		SBJCT:			
	60	QUERY:			
		SBJCT:			
	65	QUERY:	892	RGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPFMSQER	
		SBJCT:	961		1020
	70	QUERY:	952	TVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISSPLSTFFSAAPGQNPIVPE	1011
	70				

		SBJCT:	1021	TVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPVIISSPLSTFFSDAPGRNPIVPE 1	L080
				TQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPLNLIRVHLMVAVEGHLFQK	
	5			TQVLHEEIEVPGSSIKLIYLSSRTAGYKSLLKIIMTQSLVPLNLIKVHLMVAVEGHLFQK	
				SFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLILWEKRTALLQGFELD :	
	10			SFLASPNLAYTFIWDKTDAYGQKVYGLSDAVVSVGFEYETCPSLILWEKRTALLQGFELD	
		_		PSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGNGRRRSISCPSCNGLA	
	1.5			PSNLGGWSLDKHHVLNVKSGILHKGNGENQFLTQQPAVITSIMGNGRRRSISCPSCNGLA	
	15			EGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLA	
				EGNKLLAPVALAVGIDGSLFVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLA VDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFDEARCGDGGKAID	
	20			VDPVSGSLIVSDINSRRIIRVKSLSGIRDLAGNSEVVAGIGEQCDIPBLARCGSGGGTIPBLARCGSGGGTIPBLARCGSGGGTIPBLARCGSGGGGTIPBLARCGSGGGGTIPBLARCGSGGGGTIPBLARCGSGGGGGTIPBLARCGSGGGGGTIPBLARCGSGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	
				ATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQV	
	25				
				RLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKXXXXX	
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1				+	
THE SEA	30	QUERY:	1432	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	1491
The Street Street		SBJCT:	1501	+	1560
a de la companya de l	35	QUERY:	1492	GDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPGEQE	1551
As And		SBJCT:	1561	GDDGYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNRPILNSFNQYEAASPGEQE	1620
## ## ## ## ## ## ## ## ## ## ## ## ##	40	QUERY:	1552	LYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLKIRRDSSGMPRHLLMP	1611
	-			LYVFNADGIHQYTLSLVTGEYLYNFTYSSDNDVTEVMDSNGNSLKVRRDASGMPRHLLMP	
Verry game				DNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKSDETGWTTFYDYDHEGRLTN	
######################################	45			DNQIVTLAVGTNGGLKLVSTQTLELGLMTYNGNSGLLATKSDETGWTTFYDYDHEGRLTN	
•				VTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASYTVVQDQVRNSYQLCN	
	50			VTRPTGVVTSLHREMEKSTTIDIENSNRDDDVTVITNLSSVEASTIVVQDQVRNSIQECN NGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKV	
	55			TIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVN	
				+      +	
		QUERY:	: 1852	VSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYLDKSMVLLLQSQRQYI	1911
	60	SBJCT:	: 1921		1980
		QUERY:	: 1912	FEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFL	1971
	65	SBJCT:	: 1981		2040
		QUERY:	: 1972	GTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLV	2031
	70	SBJCT:	: 2041	GTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLV	2100
	. •			77	150

15966-697



The FCTR3bcde and f amino acid sequences have 1524 of 2352 amino acid residues (64%) identical to, and 1881 of 2532 residues (79%) positive with, the amino acid residues 429-2771, 93 of 157 residues (59%) identical to and 118 of 157 residues (74%) positive with amino acid residues 1-155, and 59 of 152 residues (38%) identical to and 68 of 152 residues (43%) positive with amino acid residues 211-361 of Ten-m4 [*Mus musculus*] (ptnr: GenBank Acc: BAA77399.1) (SEQ ID NO:70) (Table 3R).

# Table 3R. BLASTP of FCTR3b, c, d, e, and f against *Mus musculus* Ten-m4 - (SEQ ID NO:70)

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>GI | 4760782 | DBJ | BAA77399.1 | (AB025413) TEN-M4 [MUS MUSCULUS]
LENGTH = 2771
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	IDENTI	ries	= 1524/2352 (64%), POSITIVES = 1881/2352 (79%), GAPS = 28/2352	2 (1%)
	QUERY: 4	101	KNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRGLPP	160
5	SBJCT: 4	129	EDSFIDSGEIDVGRRASQKIPPGTFWRSQVFIDHPVHLKFNVSLGKAALVGIYGRKGLPP	188
	QUERY: 4	161	SHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYND 5	515
10	SBJCT: 4	189	SHTQFDFVELLDGRRLLTQEARSLEGPQRQSRGPVPPSSHETGFIQYLDSGIWHLAFYND	548
10	QUERY:	516	GKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQ 5	575
	SBJCT:	549	GKESEVVSFLTTAIESVDNCPSNCYGNGDCISGTCHCFLGFLGPDCGRASCPVLCSGNGQ	608
15	QUERY:	576	YSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPT	635
	SBJCT:	609	YMKGRCLCHSGWKGAECDVPTNQCIDVACSSHGTCIMGTCICNPGYKGESCEEVDCMDPT	668
20	QUERY:	636	CSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMGPDCSV	
	SBJCT:	669	CSSRGVCVRGECHCSVGWGGTNCETPRATCLDQCSGHGTFLPDTGLCNCDPSWTGHDCSI	
	QUERY:	696	EVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHC	
25	SBJCT:	729	EICAADCGGHGVCVGGTCRCEDGWMGAACDQRACHPRCAEHGTCRDGKCECSPGWNGEHC ******	
an to the	QUERY:	756	TIGRQTAGTETDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEG	
□ □ 30	SBJCT:	789	TIAHYLDRVVKEGCPGLCNGNGRCTLDLNGWHCVCQLGWRGTGCDTSMETGCGDGKDNDG	
That was	QUERY:	816	DGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVKSFYDRIKLLAGKDS	
	SBJCT:	849	DGLVDCMDPDCCLQPLCHVNPLCLGSPDPLDIIQETQAPVSQQNLNPFYDRIKFLVGRDS	
14 35 11	QUERY:	874	THIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANG	
First First \$	SBJCT:	909	THSIPGENPFDGGHACVIRGQVMTSDGTPLVGVNISFINNPLFGYTISRQDGSFDLVTNG	
<b>40</b>	QUERY:		GASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISS    +         +     +    +   +   +    +                        +   +	
mark stands	SBJCT:		GISIILRFERAPFITQEHTLWLPWDRFFVMETIVMRHEENEIPSCDLSNFARPNPVVSPS	
Ent.	QUERY:		PLSTFFSAAPGONPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPL	
[] 45			PLTSFASSCAEKGPIVPEIQALQEEIVIAGCKMRLSYLSSRTPGYKSVLRISLTHPTIPF NLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCP	
			NLTRVHLMVAVEGHLFQRSFQASPNLASTFTWDRTDAYGQRVTGLSDAVVSVGFETETCF   ++           +  +  +	
50			NLMKVHLMVAVEGRLFRKWFAAAPDLSIIFIWDKIDVINQKVFGF3EAFV3VGIEIESCF SLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSI	
			+   +	
55			MGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILEL	
33				
			RNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGE	
60			+ +  ++          +  +++      +++    +         + RNKDFRHSHSPAHKYYLATDPMSGAVFLSDTNSRRVFKVKSTTVVKDLVKNSEVVAGTGD	
			OCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSND	
65				
			LTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPM	
			+	
70			70	1506

		HCQVPGID-YSLSKXXXXXXXXXXXXXXXXXTGVLYITETDEKKINRLRQVTTNGEICLL :         +     HCQVPGIDHFLLSKVAIHATLESATALAVSHNGVLYIAETDEKKINRIRQVTTSGEISLV :	
5		AGAASXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKN	
10	QUERY: 1533	KPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNG                     +     +       +	1592
10	SBJCT: 1569	KPFLNTQNMYELSSPIDQELYLFDTSGKHLYTQSLPTGDYLYNFTYTGDGDITHITDNNG	1628
	QUERY: 1593	NSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKS	1652
15	SBJCT: 1629	NMVNVRRDSTGMPLWLVVPDGQVYWVTMGTNSALRSVTTQGHELAMMTYHGNSGLLATKS	1688
	QUERY: 1653	DETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSV +	1712
20	SBJCT: 1689	NENGWTTFYEYDSFGRLTNVTFPTGQVSSFRSDTDSSVHVQVETSSK-DDVTITTNLSAS	1747
20	QUERY: 1713	EASYTVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPME	1772
	SBJCT: 1748	GAFYTLLQDQVRNSYYIGADGSLRLLLANGMEVALQTEPHLLAGTVNPTVGKRNVTLPID	1807
25	QUERY: 1773	NGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIY	1832
	SBJCT: 1808	NGLNLVEWRQRKEQARGQVTVFGRRLRVHNRNLLSLDFDRVTRTEKIYDDHRKFTLRILY	1867
13 13 30	QUERY: 1833	DQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWS	1892
111	SBJCT: 1868	DQAGRPSLWSPSSRLNGVNVTYSPGGHIAGIQRGIMSERMEYDQAGRITSRIFADGKMWS	1927
2	QUERY: 1893	YSYLDKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESN	1952
<b>35</b>	SBJCT: 1928	YTYLEKSMVLHLHSQRQYIFEFDKNDRLSSVTMPNVARQTLETIRSVGYYRNIYQPPEGN	1987
Mary Merch	QUERY: 1953	ASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVN	2012
<b>40</b>	SBJCT: 1988	ASVIQDFTEDGHLLHTFYLGTGRRVIYKYGKLSKLAETLYDTTKVSFTYDETAGMLKTVN	2047
	QUERY: 2013	LQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLF   +   +     +   ++   +  +  +	2072
Service Servic	SBJCT: 2048	LQNEGFTCTIRYRQIGPLIDRQIFRFTEEGMVNARFDYNY-DNSFRVTSMQAVINETPLP	2106
<b>1</b> 45	QUERY: 2073	VDLYRYDETSGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMY +     ++                      +     +   +    +	2132
in it	SBJCT: 2107	IDLYRYDDVSGKTEQFGKFGVIYYDINQIITTAVMTHTKHFDAYGRMKEVQYEIFRSLMY	2166
50	QUERY: 2133	WMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXX	2192
30	SBJCT: 2167	WMTVQYDNMGRVVKKELKVGPYANTTRYSYEYDADGQLQTVSINDKPLWRYSYDLNGNLH	2226
	QUERY: 2193	XXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKA	2252
55	SBJCT: 2227	LLSPGNSARLTPLRYDLRDRITRLGDVQYKMDEDGFLRQRGGDVFEYNSAGLLIKAYNRA	2286
	QUERY: 2253	SGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGH      +     +	2312
60	SBJCT: 2287	SGWSVRYRYDGLGRRVSSKSSHSHHLQFFYADLTNPTKVTHLYNHSSSEITSLYYDLQGH	2346
00	QUERY: 2313	LFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHG	2372
	SBJCT: 2347	LFAMELSSGDEFYIACDNIGTPLAVFSGTGLMIKQILYTAYGEIYMDTNPNFQIIIGYHG	2406
65	QUERY: 2373	GLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEP-APFNLYMFKSNNPLSSELDL	2431
	SBJCT: 2407	GLYDPLTKLVHMGRRDYDVLAGRWTSPDHELWKRLSSNSIVPFHLYMFKNNNPISNSQDI	2466
70	QUERY: 2432	KNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQ	2487

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SBJCT: 2467 KCFMTDVNSWLLTFGFQLHNVIPGYPKPDTDAMEPSYELVHTQMKTQEWDNSKSILGVQC 2526
       QUERY: 2488 TTERHNQAFMALE-----GQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVT 2541
                                                  ++ + | + |
                                            + |
                                SBJCT: 2527 EVQKQLKAFVTLERFDQLYGSTITSCQQAPETKK----FASSGSIFGKGVKFALKDGRVT 2582
  5
       QUERY: 2542 TGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKV 2601
                 SBJCT: 2583 TDIISVANEDGRRIAAILNNAHYLENLHFTIDGVDTHYFVKPGPSEGDLAILGLSGGRRT 2642
  10
       QUERY: 2602 LESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQR 2661
                                                       |+|||||||+||||
                            +++|||||+|+|+|| | |+ |||
                 | | + | | | | | | | |
       SBJCT: 2643 LENGVNVTVSQINTMLSGRTRRYTDIQLQYRALCLNTRYG---TTVDEEKVRVLELARQR 2699
       OUERY: 2662 ALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSN 2721
  15
                  SBJCT: 2700 AVRQAWAREQQRLREGEEGLRAWTDGEKQQVLNTGRVQGYDGFFVTSVEQYPELSDSANN 2759
       QUERY: 2722 IQFLRQNEMGKR 2733
  20
                  | |+||+|||+|
       SBJCT: 2760 IHFMRQSEMGRR 2771
        SCORE = 161 BITS (407), EXPECT = 2E-37
        IDENTITIES = 93/157 (59%), POSITIVES = 118/157 (74%), GAPS = 4/157 (2%)
  25
                 MDVKDRR-HRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGN 59
       QUERY: 1
                 MDVKERKPYRSLTRRR-DAERRYTSSSADSEEGKGP-QKSYSSSETLKAYDQDARLAYGS 58
       SBJCT: 1
□ 30
                 RVTDLIHRESDEFPRQGTNFTLAELGICEPS-PHRSGYCSDMGILHQGYSLSTGSDADSD 118
       QUERY: 60
tij
                 RVKDMVPQEAEEFCRTGTNFTLRELGLGEMTPPHGTLYRTDIGLPHCGYSMGASSDADLE 118
L.
       SBJCT: 59
       OUERY: 119 TEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLT 155
i.
  35
                  114
       SBJCT: 119 ADTVLSPEHPVRLWGRSTRSGRSSCLSSRANSNLTLT 155
Ti.
        SCORE = 72.1 BITS (176), EXPECT = 8E-11
        IDENTITIES = 59/152 (38%), POSITIVES = 68/152 (43%), GAPS = 42/152 (27%)
C.
  40
       QUERY: 285 PAPAPND--LATTP-----ESVQLQDSWVLNSNVPLETR------ 316
L.
                                | | + | + | | | | + | | | | |
                 ###
###
        SBJCT: 211 PSPAPTDHSLSGEPPAGSAQEPTHAQDNWLLNSNIPLETRNLGKQPFLGTLQDNLIEMDI 270
LIS.
                            -HFLFKXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRKAFK 363
  45
                                              SBJCT: 271 LSASRHDGAYSDGHFLFK-PGGTSPLFCTTSPGYPLTSSTVYSPPPRPLPRSTFSRPAFN 329
        QUERY: 364 LKKPSKYCSWKCXXXXXXXXXXXXXXXXYFI 395
  50
                 SBJCT: 330 LKKPSKYCNWKCAALSAILISATLVILLAYFV 361
        *FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS
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The 997-2733 amino acid fragment of the FCTR3bcde and f protein was also found to have 1695 of 1737 amino acid residues (97%) identical to, and 1695 of 1737 residues (97%) positive with the amino a 1737 amino acid residue protein KIAA1127 protein [Homo sapiens] (GenBank Acc:(AB032953) (SEQ ID NO:71), (Table 3S).

Table 3S. BLASTP of FCTR3b, c, d, e, and f against Homo sapiens KIAA1127 protein (SEQ ID NO:71)

>GI | 6329763 | DBJ | BAA86441.1 | (AB032953) KIAA1127 PROTEIN [HOMO SAPIENS] LENGTH = 1737

5	QUERY:		TFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPLNLI	
	OHERY:	1057	RVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLI	
10	SBJCT:			
10			I.WEKRTALLOGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGN	
	SBJCT:			
15			GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILELRNK	
	SBJCT:			
20	QUERY:	1237	EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL	1296
	SBJCT:	241		300
2.5	QUERY:	1297	PFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA	1356
25	SBJCT:	301		360
## ## ## ## ## ## ## ## ## ## ## ## ##	QUERY:	1357	VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQ	1416
<b>4</b> 30	SBJCT:	361	VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQ	420
The state of the s	QUERY:	1417	VPGIDYSLSKXXXXXXXXXXXXXXXXXTGVLYITETDEKKINRLRQVTTNGEICLLAGAA	1476
== 35	SBJCT:	421	VPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINRLRQVTTNGEICLLAGAA	480
William Speed	QUERY:	1477	SXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL	1536
<b>8</b>	SBJCT:		SDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL	
[] 40 []	QUERY:	1537	NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK	
	SBJCT:		NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK	
<b>L</b> 45	QUERY:	1597	IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKSDETG	
and the second	SBJCT:		IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKSDETG	
50			WTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASY	
50	SBJCT:		WTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASY	
			TVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLN	
55	SBJCT:		TVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLN SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQVG	
	SBJCT:		SIEWRLRKEQIKGKVIIFGRKLRVHGRNLLSIDIDANIRIEKIIDDIRKHILKIIIDQVG	
60			RPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYL	
00	SBJCT:			
			DKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVI	
65	SBJCT:			
	QUERY:	1957	FDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSG	
70	SBJCT:	961		1020

```
QUERY: 2017 GFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 2076
               SBJCT: 1021 GFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 1080
  5
      QUERY: 2077 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 2136
               SBJCT: 1081 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 1140
      QUERY: 2137 QYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXXXXX 2196
 10
               SBJCT: 1141 QYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNP 1200
      QUERY: 2197 XXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 2256
                15
      SBJCT: 1201 GNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 1260
      QUERY: 2257 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAM 2316
               SBJCT: 1261 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAM 1320
 20
      QUERY: 2317 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 2376
               SBJCT: 1321 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 1380
 25
      QUERY: 2377 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 2436
               SBJCT: 1381 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 1440
      QUERY: 2437 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 2496
₩ 30
               H
      SBJCT: 1441 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 1500
200
      QUERY: 2497 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 2556
±± 35
               SBJCT: 1501 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 1560
Li
Ti,
      QUERY: 2557 SVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 2616
               SBJCT: 1561 SVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 1620
1.3
 40
QUERY: 2617 VNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKARD 2676
               Brien.
      SBJCT: 1621 VNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKARD 1680
  45
      QUERY: 2677 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR 2733
               SBJCT: 1681 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR 1737
  50
```

The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2528 of 2774 amino acid residues (91%) identical to, and 2557 of 2774 residues (92%) positive with, the 2765 amino acid residue protein neurestin alpha [Rattus norvegicus] (GenBank Acc: AF086607) (SEQ ID NO:72), shown in Table 3T.

## Table 3T. BLASTP of FCTR3bcd and f against Rattus norvegicus Neurestin alpha (SEQ ID NO:72)

```
>GI | 9910320 | REF | NP 064473.1 | NEURESTIN ALPHA [RATTUS NORVEGICUS]
GI 5712201 GB AAD47383.1 AF086607 1 (AF086607) NEURESTIN ALPHA [RATTUS NORVEGICUS]
          LENGTH = 2765
```

60 SCORE = 4988 BITS (12938), EXPECT = 0.0 IDENTITIES = 2528/2774 (91%), POSITIVES = 2557/2774 (92%), GAPS = 50/2774 (1%)

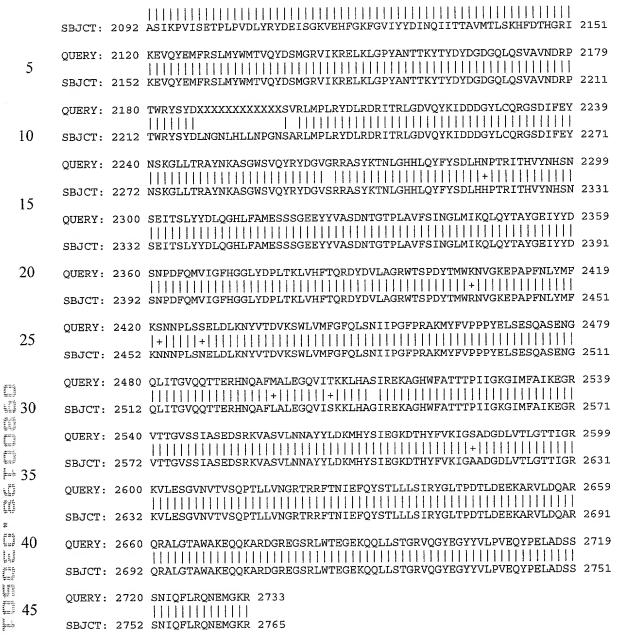
55

MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60 QUERY: 1

> 83 15966-697

		SBJCT:	1.		50
	5	QUERY:	61	VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 1	
		SBJCT:	61	VTDLVHRESDEFSRQGANFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 1	
]		QUERY:	121	GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	
	10	SBJCT:	121	GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDDNGRPIPPTSSSSLL 1	180
		QUERY:	181	XXXXXXXHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXX 2	240
1	15	SBJCT:	181	PSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP 2	240
		QUERY:	241	NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	300
		SBJCT:	241	NHHSQSTLRPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQ 3	300
2	20	QUERY:	301	LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRK 3	360
		SBJCT:	301	LQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRK	360
2	25	QUERY:	361	AFKLKKPSKYCSWKCXXXXXXXXXXXXXXXXXXXXXXXX 3	395
•		SBJCT:	361	AFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT 4	420
\$21. 2007		QUERY:	396	VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK	439
att that	30	SBJCT:	421	GLPGNDDVATVPSGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK	480
222		QUERY:	440	FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF	499
**************************************	35	SBJCT:	481	FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF	540
A.F.		QUERY:	500	VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGA	
***************************************		SBJCT:	541	VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGLCHCFPGFLGA	
	40	QUERY:	560	DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCSA (	
4 10 H 3400		SBJCT:		DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCAA	
man dent	45	QUERY:	620	GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDT (	
n in the second		SBJCT:	661	GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDS	
		QUERY:	680	GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC	
	50	SBJCT:	721	GLCNCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC ********	
		QUERY:	740	KDGKCECREGWNGEHCTIGRQTAGTETDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC	
	55	SBJCT:	781	KDGKCECREGWNGEHCTIDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC	
		QUERY:	800	NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK	
		SBJCT:	832	NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK	
	60	QUERY:	860	SFYDRIKLLAGKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYT	919
		SBJCT:	892	SFYDRIKLLAGKDSTHIIPGDNPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYT	951
	65	QUERY:	920	ITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD	979
		SBJCT:	952	ITRQDGTFDLIANGGSALTLHFERAPFMSRERTVWPPWNSFYAMDTLVMKTEENSIPSCD	1011
		QUERY:	980	LSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYK	1039
	70	SBJCT:	1012	2 LSGFVRPDPIIISSPLSTFFSASPAANPIVPETQVLHEEIELPGTNVKLRYLSSRTAGYK	1071

	5	QUERY:	1040	SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS 109	9
		SBJCT:	1072	SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 113	1
		QUERY:	1100	DAVVSVGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGE 115	9
	10			DAVVSVGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHTLNVKSGILLKGTGE 119	
				NQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 121	
				NQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLFVGDFNY1R 125	
	15	_		RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 127	
				RIFPSRNVTSILELRNKEFKHSNSPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 131	
				DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 133	
	20			DLAGNSEVVAGTGEQCLPFDEARCGDGGKAVDATLMSPRGIAVDKNGLMYFVDATMIRKV 137	
		_		DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 139	
,	25			DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 143	
				TENHQVSIIAGRPMHCQVPGIDYSLSKXXXXXXXXXXXXXXXXTGVLYITETDEKKINR 145	
225 200				TENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINR 149	
Heads Marie	30			LRQVTTNGEICLLAGAASXXXXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIA 151	
#=4 #=4				LRQVTTNGEICLLAGAASDCDCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 155	
W. 14.44	35			DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 157	
Mark State				DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 161	
Ξ	40			TDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLM 163	
				ADNOVTELIONNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKAVSTQNLELGLM 16	
mir i ii				TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 169	
	45			TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITVDIENSNR 173	
man's				DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTIT 179	
	50			DNDVTVITNLSSVEASYTVVQDQVRNSYQLCSNGTLRVMYANGMGVSFHSEPHVLAGTLT 179	
				PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 18:	
	55			PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 18	
		-		O YDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 18 	
				IVSRMFADGKVWSYSYLDKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSI 19.	
	<i>c</i> 0			TVSRMFADGKVWSYSYLDKSMVLLLQSQRQIIFEIDSSDRLLAVIMFSVARASMSINISI 19 	
	60			O GYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 19	
				GYIRNIYNPPESNASVIFDISDDGRILKISFLGIGAQVFIRIGALISKLISEIVIDSIAVII 19 	
	65			O GYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 20	
				GYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQTYRFSEEGMVMARFDTTTMDMSFKT 20	
	70			O ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 21	
	70	QUERY:	2060	N WOIVEATOETENDDIKIDETOGVAGUEGVEGATIIDIMÄTTIIMAMITDOVUEDIUGKI SI	



\* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

50

55

60

The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2536 of 2774 amino acid residues (91%) identical to, and 2558 of 2774 residues (91%) positive with, the 2764 amino acid residue protein Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc:NP\_035986.2) (SEQ ID NO:65), shown in Table 3U.

Table 3U. BLASTP of FCTR3bcde and f against Odd Oz/ten-m homolog 2 (SEQ ID NO:65)

```
>GI | 7657415 | REF | NP 035986.2 | ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M HOMOLOG

(DROSOPHILA) [MUS MUSCULUS]

GI | 4760778 | DBJ | BAA77397.1 | (AB025411) TEN-M2 [MUS MUSCULUS]

LENGTH = 2764

SCORE = 4996 BITS (12961), EXPECT = 0.0
```

	IDENTITIES	= 2536/2774 (91%), POSITIVES = 2558/2774 (91%), GAPS = 51/2774	4 (1%)
	QUERY: 1	MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR	60
5	SBJCT: 1	MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR	60
	QUERY: 61	VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE	120
10	SBJCT: 61	VTDLVHRESDEFSRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE	120
10	QUERY: 121	GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	180
	SBJCT: 121		180
15	QUERY: 181	XXXXXXXXHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXXX	240
	SBJCT: 181		240
20	QUERY: 241	NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXIHAPAPAPNDLATTPESVQ	300
20	SBJCT: 241	NHHSQSTLRPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQ	300
	QUERY: 301	LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRK	360
25	SBJCT: 301		360
	QUERY: 361	AFKLKKPSKYCSWKCXXXXXXXXXXXXXXXXYFI	395
11 1130	SBJCT: 361		420
Ţij.	QUERY: 396		439
Howard and the state of the sta	SBJCT: 421	GLPGNDDVATVPSGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK	480
¥= 35 ¥#	QUERY: 440	FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF	499
# 10 m	SBJCT: 481	FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF	540
£ 40	QUERY: 500	VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGA	559
with And	SBJCT: 541	VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGLCHCFPGFLGA	
	QUERY: 560	DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCSA	
[] 45 [=	SBJCT: 601	DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQC1DPSCGGHGSC1DGNCVCAA	
•	QUERY: 620	GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDT	
50	SBJCT: 661	GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDS	
	QUERY: 680	GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC	
	SBJCT: 721	GLCSCDPNWMGPDCSV-VCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC ********	
55	QUERY: 740	KDGKCECREGWNGEHCTIGRQTAGTETDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC	
	SBJCT: 780	KDGKCECREGWNGEHCTIDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC	
60	QUERY: 800		
	SBJCT: 831	NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK	
	QUERY: 860	SFYDRIKLLAGKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYT	
65	SBJCT: 891	SFYDRIKLLAGKDSTHIIPGDNPFNSSLVSLIRGQVVTMDGTPLVGVNVSFVKYPKYGYT	
	QUERY: 920	ITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD	
70	SBJCT: 951	ITRQDGTFDLIANGGSALTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD	
		87	150

	QUERY:		LSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYK :	
5			SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS :	
10	QUERY:	1100	DAVVSVGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGE :	1159
15			NQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR	
20			RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK	
20			DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV	
25			DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 	
30 30	SBJCT:	1431	TENHQVSIIAGRPMHCQVPGIDYSLSKXXXXXXXXXXXXXXXXTGVLYITETDEKKINR                    TENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINR	1490
1 1 1 1 1	SBJCT:	1491	LRQVTTNGEICLLAGAASXXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIA	1550
19 19 40	SBJCT:	1551	DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS	1610
and should show the short shows the	SBJCT:	: 1611	TDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLM	1670
45 Lik	SBJCT	: 1671	TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR	1730
50	SBJCT	: 1731	DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTIT	1790
55	SBJCT	: 1791	PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI	1850
60	SBJCT	: 185	YDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSIFFNGRLAGDQRGAMSERIDIDRQGR	1910
65	SBJCT	: 191	1 TVSRMFADGKVWSYSYLDKSMVLLLQSQRQYTFETDSSDRLLAVTMFSVARMSMSTHTST 	1970
0.5	SBJCT	: 197	GYIRNIYNPPESNASVIFDYSDDGRILKISFLGIGRQVFIRIGRISKISEIVIDSTAVIF	2030
70	ZORKI	. 200		150//

		SBJCT:	2031	GYDETTGVLKMVNLQSGGFSCTIRYRKVGPLVDKQIYRFSEEGMINARFDYTYHDNSFRI 2090
	5			ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2119
				ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2150
				KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2179
		SBJCT:	2151	KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2210
		QUERY:	2180	TWRYSYDXXXXXXXXXXXXXXVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2239
		SBJCT:	2211	TWRYSYDLNGNLHLLNPGNSARLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2270
	15	QUERY:	2240	NSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2299
		SBJCT:	2271	NSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2330
	20	QUERY:	2300	SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2359
	20	SBJCT:	2331	
		QUERY:	2360	SNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMF 2419
	25	SBJCT:	2391	+
		QUERY:	2420	KSNNPLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2479
<b>1</b> 3		SBJCT:	2451	+    +
211	30	QUERY:	2480	QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2539
31 ST		SBJCT:	2511	
Į.	35	QUERY:	2540	VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGR 2599
Mr. W.		SBJCT:	2571	
¥	40	QUERY:	2600	KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2659
In a series				
unt alem a				ORALGTAWAKEOOKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSS 2719
Thin, if it is				
				SNIQFLRQNEMGKR 2733
	50	SEUCI:	4 / J I	DODG NOW COMPANY WINDS AMINO ACIDS

\* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

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FCTR3 is related to rat neurestin, a gene implicated in neuronal development (Otaki JM, Firestein S Dev Biol 1999 Aug 1;212(1):165-81) Neurestin shows homology to human gammaheregulin, a Drosophila receptor-type pair-rule gene product, Odd Oz (Odz) / Ten(m), and Ten(a). Neurestin has putative roles in synapse formation and brain morphogenesis. A mouse neurestin homolog, DOC4, has independently been isolated from the NIH-3T3 fibroblasts. DOC4 is also known as tenascin M (TNM), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The significant homology to these molecules and in particular, γ-heregulin, have important implications regarding the potential contribution of FCTR3 to disease progression. Heregulin is the ligand for HER-2/ErbB2/NEU, a proto-oncogene receptor tyrosine

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kinase implicated in breast and prostate cancer progression that was originally identified in rat neuro/glioblastoma cell lines. Extopic expression of HER-2/ErbB2/NEU in MDA-MB-435 breast adenocarcinoma cells confers chemoresistance to Taxol-induced apoptosis relative to vector transfected control cells (Yu et al. Overexpression of ErbB2 blocks Taxol-induced apoptosis by up-regulation of p21Cip1, which inhibits p34Cdc2 kinase. Molec. Cell 2: 581-591, 1998).

#### FCTR3 related tenascins and cancer biology

As mentioned, FCTR3 also has significant homology to DOC4, (AKA tenascin M), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The tenascins are a growing family of extracellular matrix proteins that play prominent roles in tissue interactions critical to embryogenesis. Overexpression of tenascins has been described in multiple human solid malignancies.

The role of the tenascin family of related proteins is to regulate epithelial-stromal interactions, participate in fibronectin-dependent cell attachment and interaction. Indeed, tenascin-C (TN) is overexpressed in the stroma of malignant ovarian tumours particularly at the interface between epithelia and stroma leading to suggestions that it may be involved in the process of invasion (Wilson et al (1996) Br J Cancer 74: 999-1004). Tenascin-C is considered a therapeutic target for certain malignant brain tumors (Gladson CL: J Neuropathol Exp Neurol 1999 Oct;58(10):1029-40). Stromal or moderate to strong periductal Tenascin-C expression in DCIS (ductal carcinoma in situ) correlates with tumor cell invasion. (Jahkola et al. Eur J Cancer 1998 Oct;34(11):1687-92. Tenascin-C expression at the invasion border of early breast cancer is a useful predictor of local and distant recurrence. Jahkola T, et al. Br J Cancer. 1998 Dec;78(11):1507-13). Tenascin (TN) is an extracellular matrix protein found in areas of cell migration during development and expressed at high levels in migratory glioma cells. Treasurywala S, Berens ME Glia 1998 Oct;24(2):236-43 Migration arrest in glioma cells is dependent on the alphaV integrin subunit. Phillips GR, Krushel LA, Crossin KL J Cell Sci 1998 Apr;111 (Pt 8):1095-104 Domains of tenascin involved in glioma migration. Finally, tenascin expression in hormone-dependent tissues of breast and endometrium indicate that Tenascin expression reflects malignant progression and is down-regulated by antiprogestins during terminal differentiation of rat mammary tumors (Vollmer et al. Cancer Res 1992 Sep 1;52(17):4642-8)

#### Potential role of FCTR3 in oncologic disease progression:

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Based on the bioactivity described in the medical literature for related molecules, FCTR3 may play a role in one or more aspects of tumor cell biology that alter the interactions of tumor epithelial cells with stromal components. In consideration, FCTR3 may play a role in the following malignant properties:

Autocrine/paracrine stimulation of tumor cell proliferation

Autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy

Local tissue remodeling, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis.

Tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance.

# Therapeutic intervention targeting FCTR3 in oncologic and central nervous system indications:

Predicted disease indications from expression profiling in 41 normal human tissues and 55 human cancer cell lines (see Example 2) include a subset of human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas. Targeting of FCTR3 by human or humanized monoclonal antibodies designed to disrupt predicted interactions of FCTR3 with its cognate ligand may result in significant antitumor/anti-metastatic activity and the amelioration of associated symptomatology. Identification of small molecules that specifically/selectively interfere with downstream signaling components engaged by FCTR3/ligandinteractions would also be expected to result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Likewise, modified antisense ribonucleotides or antisense gene expression constructs (plasmids, adenovirus, adeno-associated viruses, "naked" DNA approaches) designed to diminish the expression of FCTR3 transcripts/messenger RNA (mRNA) would be anticipated based on predicted properties of FCTR3 to have anti-tumor impact.

Based on the relatedness to neurestin and heregulins, as well as its high level expression in brain tissue, FCTR3 may also be used for remyelination in order to promote regeneration/repair/remyleination of injured central nervous system cells resulting from ischemia, brain trauma and various neurodegenerative diseases.. This postulate is based on reports indicating that neuregulin, glial growth factor 2, diminishes autoimmune demyelination and enhances remyelination in a chronic relapsing model for multiple sclerosis (Cannella et al. .

Proc. Nat. Acad. Sci. 95: 10100-10105, 1998). The expression of the related molecule neurestin can be induced in external tufted cells during regeneration of olfactory sensory neurons.

#### FCTR4

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FCTR4 is a plasma membrane protein related to NF-Kappa-B P65delta3 protein. The clone is expressed in fetal liver tissues.

The novel FCTR4 nucleic acid of 609 nucleotides (also referred to as 29692275.0.1) is shown in Table 4A. An ORF begins with an ATG initiation codon at nucleotides 99-101 and ends with a TAA codon at nucleotides 522-524. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 4A, and the start and stop codons are in bold letters.

### Table 4A. FCTR4 Nucleotide Sequence (SEQ ID NO:14)

The FCTR4 protein encoded by SEQ ID NO:14 has 141 amino acid residues and is presented using the one-letter code in Table 4B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the plasma membrane with a certainty of 0.6000. The most likely cleavage site for a peptide is between amino acids 39 and 40, *i.e.*, at the dash in the amino acid sequence ACT-CCA, based on the SignalP result. The predicted molecular weight of this protein is 16051.5 Daltons.

#### Table 4B. Encoded FCTR4 protein sequence (SEQ ID NO:15).

 ${\tt MNECMNEWTDNPQAKDLHDLPLPSFHFILTSTNTKSPSYVNTICTFMAPCFVICCSLCLEYKLSKYHPHFKIFSRKLPLSTPTLPPPPRVSQSFLCATFVPVSTVALIKLHCVSHFLDCELFEAEDYLFISLPPMPRTGPS$ 

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR4 protein showed 30 % identities (22 over 72 amino acids) and 43% homologies (31 over 72 amino acids) with hypothetical 10 kD protein of *Trypanosoma cruz*i (86 aa; ACC:Q99233) shown in Table 4C. The best homologies with a human protein were 54 % identities (114 over 343 amino acids) with NF-Kappa-B P65delta3 protein (71 aa fragment; ACC:Q13313) (SEQ ID NO:77).

### Table 4C. BLASTP of FCTR4 against protein sequences

BLAST X search results are shown below:

ptnr:SPTREMBL-ACC:Q99233 HYPOTHETICAL 10 KD PROTEIN +3, 68, 0.60, 1, (SEQ ID

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NO:73) ptnr:SPTREMBL-ACC:Q16896 GABA RECEPTOR SUBUNIT - AEDES +3, 66, 0.81, 4 (SEQ ID NO:74) ptnr:SPTREMBL-ACC:O76473 GABA RECEPTOR SUBUNIT - LEPTI... +3, 66, 0.99, 2 (SEQ ID NO:75) ptnr:TREMBLNEW-ACC:AAD28317 F13J11.13 PROTEIN - Arabid... +3, 62, 0.99, 1 (SEQ ID NO:76)

Based upon homology, FCTR4 proteins and each homologous protein or peptide may share at least some activity.

#### FCTR5

FCTR5 is a protein bearing sequence homology to human complement C1R component precursor. The clone is expressed in breast, heart, lung, fetal lung, salivary gland, adrenal gland, spleen, kidney, and fetal kidney.

The novel FCTR5 nucleic acid of 1667 nucleotides (also referred to as 32125243.0.21) is shown in Table 5A. An ORF begins with an ATG initiation codon at nucleotides 34-36 and ends with a TGA codon at nucleotides 1495-1497. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 5A, and the start and stop codons are in bold letters.

## Table 5A. FCTR5a Nucleotide Sequence (SEQ ID NO:16)

 $\underline{\texttt{GTTCTCTCGCAGGTCCCAGATGTCCAGTTCCAG}} \textbf{ATG} \texttt{CCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCCCTCAG}$ TCTTGGCCCAAGAGCTACCCCAGCAGCTGACATCCCCCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACG GGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCACTGCCAGGAGCCCTATTATCAGGCCG  ${\tt CCTGTCTGCGGACGGCCAGTCACCCCCATTGCCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCAACTT}$ A CACCATCTACCCCAAGGACAGTGTTTCTCTCAGGAAGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGGGGAACCACCCTGTCCACCGTGTCGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATAACTT AAGTACTCGAGGCTGCCTGTAGCTCCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACACAGACCCCGAGGTGTTTTC  $\tt TGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGGACAGTGGCAGCCTCTATGTGGTAT$  ${\tt ACCAAGGTGCTCAGCTATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAAT{\tt TGA}\underline{\tt CCCTGGGGGGCTTGAACAGGGACT}$ 

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The FCTR5 protein encoded by SEQ ID NO:16 has 487 amino acid residues, and is presented using the one-letter code in Table 5B. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5 protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

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#### Table 5B. Encoded FCTR5a protein sequence (SEQ ID NO:17).

MPGPRVWGKYLWRSPHSKGCPGAMWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVFQDF
DLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPIS
EASRGSEAINAPGDNPAKVQNHCQEPYYQAAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIAQNQTTLGSSRAKLGNFPW
QAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVNVFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLE
LQHSIPLGPNVLPVCLPDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMFCVGDETQRHS
VCOGDSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN

An alternative embodiment, FCTR5b, is a 1691 base sequence shown in Table 5C.

### Table 5C. FCTR5b Nucleotide Sequence (SEQ ID NO:18)

TTTTTTTTAAAAAAAAAAAAAAAGGGAAATCCTATTCACATCACTGTTGCACCAAGCCACTGCAAGAGAAACCCCCACCCCCT AATTCTTGCCATTCATCACTCCCTTGATCCAGTCCACATAGCTGAGCACCTTGGTGTAGAAGTCATACCCTTCGCCACACCCTATG ACTGTGCCTTTGCGTCTCATCCCCAACACAGAACATATTGTCAGAAAACACCTCGGGTCTCTGTCTCTTTTGGAGCCAGGCGTTGC  $\tt CTCCAGGAGGGCGATGTCCCCGCTAAAGTTATGGGACTCATTCTGACGGTAGTCGGGGTGCACAACGACACGGTGGACAGGGTGGT$  ${\tt TCCCCAGITTCAGCATCTATGGCTGTGTGGCCCAAGAACACTTCACACTCTGGTTCTTCCTGAGAGAAACACTGTCCTTG}$ GGGTAGATGGTGTGGGCAGCAGTGAGGATCCATCTGTCCCCCAGCAGGGCCCCGCCCCCACGGCCGTGGATACTGGTGAAGGCTTG AAGGCTGTGTGCGGAAGGTCAGCCGCAAACTCCTCCCTGAGGATACAAACTCCCTCTGACCAGGGGGCCTGCCCAGAGGGGAGCCT $\tt TGCTGACCACAGAACTGGCTTGGATCCGAACCGACGAATGAGATTGTGACAGAGTCCCTGCACAGTCCTGGGACGGCTCCAGGTCAGGTCAGGTCAGGAGAGGTCA$ GGTACCCGGGGGATGTCAGCTGCTGGGGTAGCTCTTGGGCCAAGAGGACGCGCGGGTTGGGCAAGCCTGGAGGACTCCCCAG A GAAG CAG CCACACTTG CG CCTGGACAG CCTTTG GAGTGAGGG CTTCTCCAGAGATATTTCCCCCACACTCTG GGTCCAGGCATCTGGAACTGGACATCTGGGACCTGCGAGAGAACTGGCCCAGGATAGGGAACAAAAGG

The FCTR5b protein encoded by SEQ ID NO:18 has 487 amino acid residues, and is presented using the one-letter code in Table 5D. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5b protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

#### Table 5D. Encoded FCTR5b protein sequence (SEQ ID NO:19).

45 mpgprvwgkylwrsphskgcpgamwullwgvlqacptrgsvllaqqlpqqltspgypepygkgqesstdikapegfavrlvfqdf dlepsqdcagdsvtisfvgsdpsqfcgqqgsplgrppgqrefvssgrslrltfrtqpssenktahlhkgflalyqtvavnysqpis easrgseainapgdnpakvqnhcqepyyqaaaagaltcatpgtwkdrqdgeevlqcmpvcgrpvtpiaqnqttlgssraklgnfpw qaftsihgrgggallgdrwiltaahtiypkdsvslrknqsvnvflghtaidemlklgnhpvhrvvvhpdyrqneshnfsgdialle lqhsiplgpnvlpvclpdnetlyrsgllgyvsgfgmemgwlttelkysrlpvapreacnawlqkrqrpevfsdnmfcvgdetqrhs vcqgdsgslyvvwdnhahhwvatgivswgigcgegydfytkvlsyvdwikgvmngkn

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR5a protein showed 58 % identities (177 over 302 amino acids) and 74 % homologies (226 over 302 amino acids) with human complement C1R component precursor (EC 3.4.21.41) (705 aa.; ACC:P00736). Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

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In a search of sequence databases, it was found, for example, that the nucleic acid sequence the nucleotides 17-1594 of FCTR5a have 1575 of 1578 bases (99 %) identical to Homo sapiens complement C1r-like proteinase precursor (GENBANK-ID: XM 007061.1) (SEQ ID NO:78) (Table 5E).

# Table 5E. BLASTN of FCTR5a against Homo sapiens complement C1r-like proteinase precursor (SEO ID NO:78)

>G] |11436767|REF|XM\_007061.1| HOMO SAPIENS COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, (LOC51279)

```
15
              LENGTH = 3318
       SCORE = 3104 BITS (1566), EXPECT = 0.0
IDENTITIES = 1575/1578 (99%)
       STRAND = PLUS / PLUS
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 20
CAGATGTCCAGTTCCAGATGCCTGGACCCAGAGTGTGGGGGGAAATATCTCTGGAGAAGCC 76
      QUERY: 17
               CAGATGTCCAGTTCCAGATGCCTGGACCCAGAGTGTGGGGGGAAATATCTCTGGAGAAGCC 60
      SBJCT: 1
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               CTCACTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 136
 25
      QUERY: 77
10
               CTCACTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 120
      SBJCT: 61
Hart and Hart Hart
               CTTGCCCAACCCGGGGCTCCGTCCTCTTGGCCCAAGAGCTACCCCAGCAGCTGACATCCC 196
      QUERY: 137
  30
               CTTGCCCAACCCGGGGCTCCTCTTTGGCCCAAGAGCTACCCCAGCAGCTGACATCCC 180
      SBJCT: 121
               CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCACCAGGACATCAAGGCTCCAG 256
      QUERY: 197
               35
               CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACGGACATCAAGGCTCCAG 240
      SBJCT: 181
               AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 316
      QUERY: 257
                AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 300
      SBJCT: 241
  40
               CAGGGGACTCTGTCACAATCTCATTCGTCGGTTCGGATCCAAGCCAGTTCTGTGGTCAGC 376
      QUERY: 317
                CAGGGGACTCTGTCACAATCTCATTCGTCGGTTCGGATCCAAGCCAGTTCTGTGGTCAGC 360
      SBJCT: 301
  45
               AAGGCTCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 436
       QUERY: 377
                AAGGCTCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 420
       SBJCT: 361
               TGCGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCCACCTCCACAAGG 496
       QUERY: 437
  50
                TGCGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCCACCTCCACAAGG 480
       SBJCT: 421
               GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 556
       QUERY: 497
                55
               GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 540
       SBJCT: 481
               GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCACT 616
       QUERY: 557
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		SBJCT:	541	GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACCACCTGCCAAGGTCCAGAACCACT	600
	5	QUERY:		GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCCAGGGA	
		SBJCT:	601	GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCCAGGGA	
		QUERY:		CCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGTATGCCTGTCTGCGGACGGC	
		SBJCT:			
		QUERY:		CAGTCACCCCCATTGCCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCA	
	15			ACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCCGGGGCCCTGCTGGGGG	
		QUERY:		ACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCCGTGGGGGCCCTGCTGGGGG	
		SBJCT:			
	20	QUERY:	857	ACAGATGGATCCTCACTGCCCCACACCATCTACCCCAAGGACAGTGTTTCTCTCAGGA	
		SBJCT:	841	ACAGATGGATCCTCACTGCTGCCCACACCGTCTACCCCAAGGACAGTGTTTCTCTCAGGA	
		QUERY:	917	AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG	976
	25	SBJCT:	901	AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG	960
		QUERY:	977	GGAACCACCCTGTCCACCGTGTCGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATA	1036
	20	SBJCT:	961	GGAACCACCCTGTCCACCGTGTCGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATA	1020
	30	QUERY:	1037	ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACG	1096
104 H. H.		SBJCT:	1021	ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACG	1080
-	35	QUERY:	1097	TCCTCCCGGTCTGTCTGCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTTGGGCTACG	1156
Hall Hall		SBJCT:	1081	TCCTCCCGGTCTGTCTGCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTTGGGCTACG	1140
£	40	QUERY:	1157	TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC	1216
the state	40	SBJCT:	1141	TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC	1200
Hart Hans		QUERY:	1217	CTGTAGCTCCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACACAGAGACCCGAGGTGT	1276
F.	45	SBJCT:	1201	CTGTAGCTCCCAGGGAGGCCTGCAAACGCCTGCCCAAAAGAGACACAGAGACCCGAGGTGT	1260
ş.		QUERY:	1277	TTTCTGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG	1336
	50	SBJCT:	1261	TTTCTGACAATATGTTCTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG	1320
	50	QUERY:	1337	ACAGTGGCAGCCTCTATGTGGTATGGGACAATCATGCCCATCACTGGGTGGCCACGGGCA	1396
		SBJCT:	1321		1380
	55	QUERY:	1397	TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT	1456
		SBJCT:	1381		1440
	60	QUERY:	1457	ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG	1516
		SBJCT:	1441		1500
	65	QUERY:	1517	GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT	1576
		SBJCT:	1501		1560
		QUERY:	1577	GGGGTAGGGGGT 1594	
	70	SBJCT:	1561		

In this search it was also found that the FCTR5a nucleic acid had homology to three fragments of *Homo sapiens* complement component 1, r subcomponent. It has 102 of 117 bases (87%) identical to 1458-1574, 82 of 94 bases (87%) identical to 2052-2145, and 54 of 63 bases (85%) identical to 1678-1740 all fragments of *Homo sapiens* complement component 1, r subcomponent (GenBank Acc: NM\_001733.1) (Table 5F).

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# Table 5F. BLASTN of FCTR5a against *Homo sapiens* complement component 1, r subcomponent (SEO ID NO:79)

```
>GI 4502492 REF NM_001733.1 HOMO SAPIENS COMPLEMENT COMPONENT 1, R SUBCOMPONENT
       (C1R), MRNA
  10
              LENGTH = 2386
             113 BITS (57), EXPECT = 3E-22
       SCORE =
       IDENTITIES = 102/117 (87%)
       STRAND = PLUS / PLUS
  15
      QUERY: 783 AGCCAAGCTGGGCAACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGGCGG 842
                GGCCCTGCTGGGGGACAGATGGATCCTCACTGCTGCCCACACCATCTACCCCAAGGA 899
  20
                SBJCT: 1518 GGCCCTGCTGGGCGACCGCTGGATCCTCACAGCTGCCCACACCCTGTATCCCAAGGA 1574
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25
      SCORE = 91.7 BITS (46), EXPECT = 1E-15
IDENTITIES = 82/94 (87%)
       STRAND = PLUS / PLUS
.
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       QUERY: 1380 CTGGGTGGCCACGGGCATTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTA 1439
TI 30
                SBJCT: 2052 CTGGGTGGCCACGGGCATCGTGTCCTGGGGCATCGGGTGCAGCAGGGGCTATGGCTTCTA 2111
Li
       QUERY: 1440 CACCAAGGTGCTCAGCTATGTGGACTGGATCAAG 1473
and:
                5 35
       SBJCT: 2112 CACCAAAGTGCTCAACTACGTGGACTGGATCAAG 2145
Stone.
1
       SCORE = 54.0 BITS (27), EXPECT = 2E-04
        IDENTITIES = 54/63 (85%)
  40
       STRAND = PLUS / PLUS
       QUERY: 1006 CACCCCGACTACCGTCAGAATGAGTCCCATAACTTTAGCGGGGACATCGCCCTCCTGGAG 1065
                                              SBJCT: 1678 CACCCGGACTACCGTCAGGATGAGTCCTACAATTTTGAGGGGGGACATCGCCCTGCTGGAG 1737
  45
       QUERY: 1066 CTG 1068
                SBJCT: 1738 CTG 1740
```

The amino acid sequence of the protein of FCTR5a 485 of 487 amino acid residues (99%) identical to, and 487 of 487 residues (100%) positive with, the 487 amino acid complement C1r-like proteinase precursor from *Homo sapiens* (GenBank-ACC: AAF44349.1) (SEQ ID NO:80) (Table 5G).

# Table 5G. BLASTP of FCTR5a and b against Complement C1R-like proteinase precursor (SEO ID NO:80)

```
>GI|7706083|REF|NP 057630.1| COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, [HOMO SAPIENS]
       GI 11436768 REF XP 007061.1 COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, [HOMO SAPIENS]
       GI 7271475 GB AAF44349.1 AF178985_1 (AF178985) COMPLEMENT C1R-LIKE PROTEINASE
  5
       PRECURSOR [HOMO SAPIENS]
              LENGTH = 487
              972 BITS (2513), EXPECT = 0.0
       IDENTITIES = 485/487 (99%), POSITIVES = 487/487 (100%)
  10
                                                   R
               MPGPRVWGKYLWRSPHSKGCPGAMWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEP 60
       QUERY: 1
               MPGPRVWGKYLWRSPHSKGCPGAMWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEP 60
       SBJCT: 1
  15
               YGKGQESSTDIKAPEGFAVRLVFQDFDLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLG 120
       QUERY: 61
               YGKGQESSTDIKAPEGFAVRLVFQDFDLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLG 120
       SBJCT: 61
       OUERY: 121 RPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPISEASRGSEA 180
  20
                SBJCT: 121 RPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPISEASRGSEA 180
       QUERY: 181 INAPGDNPAKVQNHCQEPYYQAAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIA 240
  25
                SBJCT: 181 INAPGDNPAKVQNHCQEPYYQAAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIA 240
¥.
       QUERY: 241 QNQTTLGSSRAKLGNFPWQAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVN 300
druk strak derti
                SBJCT: 241 QNQTTLGSSRAKLGNFPWQAFTSIHGRGGGALLGDRWILTAAHTVYPKDSVSLRKNQSVN 300
  30
       QUERY: 301 VFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLELQHSIPLGPNVLPVCL 360
ļ.i
                17
       SBJCT: 301 VFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLELQHSIPLGPNVLPVCL 360
111 35
       QUERY: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMF 420
Ŧ
                1.3
       SBJCT: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMF 420
71
       OUERY: 421 CVGDETORHSVCOGDSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480
  40
                SBJCT: 421 CVGDETQRHSVCQGDSGSVYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480
QUERY: 481 GVMNGKN 487
  45
                SBJCT: 481 GVMNGKN 487
       R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE HOMOLOGY
       IS THE SAME.
```

The full amino acid sequence of the protein of FCTR5a has 175 of 303 amino acid residues (58%) identical to, and 226 of 303 residues (74%) positive with the 400-701 amino acid segment, 72 of 157 residues (45%) identical and 94 of 157 residues (59%) positive with amino acids 1-155, and 36 of 139 residues (25%) identical and 58 of 139 residues (40%) positive with amino acids 188-312 of the 705 amino acid Complement C1R Component Precursor from *Homo sapiens* (GenBank-ACC: AAA51851.1) (SEQ ID NO:43) (Table 5H).

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## Table 5H. BLASTP of FCTR5a and b against Complement C1R Component Precursor (SEO ID NO:81)

```
>GI|115204|SP|P00736|C1R HUMAN COMPLEMENT C1R COMPONENT PRECURSOR
        GI 67614 PIR | C1HURB COMPLEMENT SUBCOMPONENT C1R (EC 3.4.21.41) PRECURSOR - HUMAN
   5
        GI 179644 GB AAA51851.1 (M14058) HUMAN COMPLEMENT C1R [HOMO SAPIENS]
                LENGTH = 705
        SCORE = 361 BITS (928), EXPECT = 8E-99
        IDENTITIES = 175/303 (58%), POSITIVES = 226/303 (74%), GAPS = 9/303 (2%)
  10
       QUERY: 189 AKVQNHCQEPYYQ------AAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIA 240
                                       | || | ||+++|+|||+||+
                 |++| +| |||+
       SBJCT: 400 ARIQYYCHEPYYKMQTRAGSRESEQGVYTCTAQGIWKNEQKGEKIPRCLPVCGKPVNPVE 459
  15
       QUERY: 241 QNQTTLGSSRAKLGNFPWQAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVN 300
                 SBJCT: 460 QRQRIIGGQKAKMGNFPWQVFTNIHGRGGGALLGDRWILTAAHTLYPKEHEA-QSNASLD 518
       QUERY: 301 VFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLELQHSIPLGPNVLPVCL 360
  20
                 SBJCT: 519 VFLGHTNVEELMKLGNHPIRRVSVHPDYRQDESYNFEGDIALLELENSVTLGPNLLPICL 578
       QUERY: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMF 420
  25
                 + + | ++ | | | | | | + | | | | | | + | + | | | | | | | | | |
       SBJCT: 579 PDNDTFYDLGLMGYVSGFGVMEEKIAHDLRFVRLPVANPQACENWLRGKNRMDVFSQNMF 638
1
F.
        QUERY: 421 CVGDETQRHSVCQGDSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480
10 mg
                          ++
        SBJCT: 639 CAGHPSLKQDACQGDSGGVFAVRDPNTDRWVATGIVSWGIGCSRGYGFYTKVLNYVDWIK 698
  30
OUERY: 481 GVM 483
hek
11
        SBJCT: 699 KEM 701
  35
ti
        SCORE = 122 BITS (306), EXPECT = 1E-26
F#2
         IDENTITIES = 72/157 (45%), POSITIVES = 94/157 (59%), GAPS = 3/157 (1%)
u
        QUERY: 24 MWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF 83
  40
200
                           | ||+ + |+| ++||| +|+||
                                                      [++] | |+ |+||
                  Hone Hall
                 MWLLYLLVPALFCRAGGSIPIPQKLFGEVTSPLFPKPYPNNFETTTVITVPTGYRVKLVF 60
        SBJCT: 1
                 ODFDLEPSODCAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTQP 143
        OUERY: 84
  45
                                         QQFDLEPSEGCFYDYVKISADKKSLGRFCGQLGSPLGNPPGKKEFMSQGNKMLLTFHTDF 120
        SBJCT: 61
        QUERY: 144 SS-ENKTAHLHKGFLALYQTVAVNYSQPISEASRGSE 179
                  |+ || | + || || || || + | + || + || ||
        SBJCT: 121 SNEENGTIMFYKGFLAYYQ--AVDLDECASRSKSGEE 155
  50
        SCORE = 36.3 BITS (83), EXPECT = 0.93
         IDENTITIES = 36/139 (25%), POSITIVES = 58/139 (40%), GAPS = 17/139 (12%)
  55
                           R
        QUERY: 35 ACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF-QDFDLEPSQD 93
                      ++| || |
                                               + |+ | + | + | |++
        SBJCT: 188 SCOAECSSELYTEASGYISSLEYPRSYPPDLRCNYSIRVERGLTLHLKFLEPFDIDDHQQ 247
  60
                  --CAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTQPSSENKTAH 151
        OUERY: 94
                    SBJCT: 248 VHCPYDQLQIYANGKNIGEFCGKQ-----RPP---DLDTSSNAVDLLFFTDESGDS---- 295
        QUERY: 152 LHKGFLALYQTVAVNYSQP 170
  65
                   + + + + +
        SBJCT: 296 -- RGWKLRYTTEIIKCPQP 312
```

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R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE HOMOLOGY IS THE SAME.

Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

#### FCTR6

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The novel nucleic acid of 1078 nucleotides FCTR6a (also designated 27455183.0.19) encoding a novel human blood coagulation factor XI-like protein is shown in Table 6A. An ORF was identified beginning with an ATG initiation codon at nucleotides 243-245 and ending with a TAA codon at nucleotides 1044-1046. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6A, and the start and stop codons are in bold letters.

### Table 6A FCTR6a Nucleotide Sequence (SEQ ID NO:20)

The FCTR6a protein encoded by SEQ ID NO:20 has 267 amino acid residues and is presented using the one-letter code in Table 6B. FCTR6a was searched against other databases using SignalPep and PSort search protocols. The FCTR6a protein is most likely mitochondrial matrix space (Certainty= 0.4372) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR6a protein is 29412.8 daltons.

### Table 6B. Encoded FCTR6a protein sequence (SEQ ID NO:21).

MGFRFLGTANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLDDL KVPICLPTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCT PEPGEKWYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEKVTQLGGRPFNAEKRRTSVKQKPMGSPVSGVPEPGSPRSWLLLCPLS HVLFRAILY

In an alternative embodiment, FCTR6b (alternatively referred to as 27455183.0.145) has the 1334 residue sequence shown in Table 6C. An ORF was identified beginning with an ATG initiation codon at nucleotides 499-501 and ending with a TAA codon at nucleotides 1300-1302. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6C, and the start and stop codons are in bold letters.

## Table 6C FCTR6b Nucleotide Sequence (SEQ ID NO:22)

GATTTTAGAAGGTTAATCAAAAACCCGGGGACAGTTTCTTCATGGCATAACCACAGACCTTTGTGGCACCCGCTGT  $\underline{CGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTATTACTGAAGATCCTGTCTGGTCAGTGGCAGGTCCTGTCTGGTCAGTGGCAGGTCCTGTCTGGTCAGTGGCAGGTCCTGGTCAGTGGCAGGTCCTGTCTGGTCAGTGGCAGGTCCTGGTCAG$  $\underline{CTATCTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAACCCAGCTCGGCCTTTG}$ 5 CTGTATTAGACAGAAGCACCTCATTCATATCCCTGGGGCCCCTGATGGTGCAGTGGTCTGGCTGTGGTCTGCACACCAGC  $\underline{\mathtt{TATTCTGTTTTGTTTTGTTTTTTTTTTTTCCTACCTTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAG}$ 10  $\tt GTGCCAATGGTCATCATGGACTGGGAGGGGGGGTGTTCAAAGATGTTTCCAAAACTTACCAAAAATATGCTGTGTGCCGGATA$ 15 AACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCAGGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAA  ${\tt ACCTATGGGCTCCCCAGTCTCGGGAGTCCCAGAGCCAGGCCAGATCCTGGCTCTGTCCCCTGTCCCATG}$  ${\tt TGTTGTTCAGAGCTATTTTGTAC{\tt TGA}\underline{{\tt TAATAAAATAGAGGCTATTCTTTCAACCGAAA}}$ 

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The FCTR6b protein encoded by SEQ ID NO:22 has 267 amino acid residues and is presented using the one-letter code in Table 6B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the mitochondrial matrix space (Certainty=0.4372). The predicted molecular weight of this protein is 29498.9 Daltons.

### Table 6D. Encoded FCTR6b protein sequence (SEQ ID NO:23).

MGFRFLGTANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLDDL
KVPICLPTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCT
PEPGEKWYQVGIISWGKSCGEKNTPGIYTSLVNYNLWIEKVTQLEGRPFNAEKRRTSVKQKPMGSPVSGVPEPGSPRSWLLLCPLS
HVLFRAILY

In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 853 of 897 bases (95 %) identical to bases 551-1447, and 346 of 388 bases (89%) identical to bases 127-513 of *Macaca fascicularis* brain cDNA, clone QccE-17034 (GENBANK-ID: |AB046651) (Table 6E).

# Table 6E. BLASTN of FCTR6a against *Macaca fascicularis* brain cDNA, clone QccE-17034 (SEO ID NO:82)

```
>GI|9651112|DBJ|AB046651.1|AB046651 MACACA FASCICULARIS BRAIN CDNA, CLONE QCCE-17034
            LENGTH = 1746
40
     SCORE = 1429 BITS (721), EXPECT = 0.0
     IDENTITIES = 853/897 (95%)
     STRAND = PLUS / PLUS
             CCTTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCCTAGA 493
    OUERY: 434
45
              CCTTTTTCCAATCCTCACACCTTCTGAGCTACAGCCCCAGTAGGGTCTAAATGTCCTAGA 610
    SBJCT: 551
             GCTACATGGGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTC 553
    QUERY: 494
              GCTATATGAGATTTAGGTTTCTGAGCACAGCCAATTCTCCCACTTTTGAGGCTTCCCTTC 670
50
    SBJCT: 611
              CCCTTCCACTTGCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCGTGC 613
    OUERY: 554
```

	SBJCT: 671 C	CCCTTTCACTCGCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAATGTCGTGC 730
	~	TGGGGACCAACGACTTAACTAGCCCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTC 673
5	SBJCT: 731 T	rggggaccaacgacttaactagctcatccatggaaataaaggaggtcgccagcatcattc 790
	~	TTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGCTT 733
10	SBJCT: 791 T	TTCACAAGGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCCT 850
	~	CGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTG 793
		CGCCCATCACACTCGATGACCTGAAGGTGCCCATCTGCCTCCCTACGCAGCACGGCCCCG 910
15	~	CCACATGGCGCGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACT 853
		CCACATGGCACGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACT 970
20	~	CTGTGAAAACGGATCTGATGAAAGTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAA 913
		CTGTGAAAACGGATCTGATGAAAGCGCCGATGGTCATCATGGACTGGGAGGAGTGTTCAA 1030 AGATGTTTCCAAAAACTTACCAAAAATATGCTGTGTGCCGGATACAAGAATGAGAGCTATG 973
25	~	AGATGTTTCCAAAACTTACCAAAAATATGCTGTGTGCCGGATACAAGAATGAGAGCTATG 5/5
23		ATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGT 1033
	•	A GCC GCAAGG TO ACT TO THE ACCCCTAGE CONTROL TO THE ACCCCTAGE GCT GCACCCCAGAGCCT GCAGAGAAGT 1150
<b>41 30</b>	OUEDV: 1034	GGTACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCCAGGGA 1093
Bridge Bridg Bri		
<b>L</b> 1 35	QUERY: 1094	TATACACCTCGTTGGTGAACTACAACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCA 1153
April 1	SBJCT: 1211	TATACACCTCGTTGGTGAACTACAACCTCTGGATCGAGAAGGTGACCCAGCTAGAGGGCA 1270
8		GGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAAACCTATGGGCTCCCCAG 1213
11 40		GGCCCTTCAGTGCGGAGAAAATGAGGACCTCTGTCAAACAGAAACCTATGGGCTCCCGAG 1330 TCTCGGGGAGTCCCAGAGCCAGAGCCCCAGATCCTGGCTCCTGTCCCCTGTCCC 1273
A SE SECTION OF THE S		
<b>1</b> 45		ATGTGTTGTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACC 1330
a in	~	ATGTGTTGTACAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTTTTTAACC 1447
50		28 BITS (216), EXPECT = E-117
	IDENTITIES STRAND = PI	= 346/388 (89%), GAPS = 1/388 (0%)
	QUERY: 1	GATTTTAGAAGGTTAATCAAAAACCCGGGGACAGTTTCTTCATGGCATAACCACAGACCT 60
55	SBJCT: 127 (	
	QUERY: 61	TTGTGGCACCCGCTGTCGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTAT 120
60	SBJCT: 187 T	
		PACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTCTAGACTAACTTCTGGTCCTGAGTT 180
65	SBJCT: 247	
03	* =	TCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATG
	SBJCT: 306	
70	QUERY: 241	CTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAA 300



In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 295 of 378 bases (78 %) identical to bases 410-779 of *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (GENBANK-ID:AK09660) (Table 6F).

# Table 6F. BLASTN of FCTR6a against *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (SEQ ID NO:83)

>GI|12855429|DBJ|AK016601.1|AK016601 MUS MUSCULUS ADULT MALE TESTIS CDNA, RIKEN FULL-LENGTH ENRICHED 20 LIBRARY, CLONE: 4933401F05, FULL INSERT SEQUENCE LENGTH = 1047SCORE = 97.6 BITS (49), EXPECT = 2E-17IDENTITIES = 295/378 (78%), GAPS = 8/378 (2%) Marie Meri 25 STRAND = PLUS / PLUS ř., QUERY: 697 AACATGGACAATGACATTGCCTTGCTGCTGCTTCGCCCCATCAAGCTCGATGACCTG 756 125 SBJCT: 410 AACATGGACAACGACATTGCCTTGTTGCTGCTAGCCAAGCCCTTGACGTTCAATGAGCTG 469 30 Til. QUERY: 757 AAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTGCCACATGGCGCGAATGCTGGGTG 816 Til. SBJCT: 470 ACGGTGCCCATCTGCCTTCCTCTGGCCCGCCCCTCCCAGCTGGCACGAATGCTGGGTG 529 35 GCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACTCTGTGAAAAACGGATCTGATGAAA 876 QUERY: 817 | | | | | | | 111 SBJCT: 530 GCAGGATGGGGCGTAACCAACTCAACTGACAAGGAATCTATGTCAACGGATCTGATGAAG 589 Hinn, GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAAGTTTTCCAAAACTTACCAAA 936 QUERY: 877 40 Lak SBJCT: 590 GTGCCCATGCGTATCATAGAGTGGGAGGAATGCTTACAGATGTTTCCCAGCCTCACCACA 649 QUERY: 937 AATATGCTGTGTGCCGGATACAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGG 996 45 SBJCT: 650 AACATGCTGTGTGCCTCATATGGTAATGAGAGCTACGATGCTTGC-QUERY: 997 GGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGTGGTACCAGGTGGGCATCATCAGC 1056 SBJCT: 702 GGACCGCTTGTCTGCACCACAGATCCTGGCAGTAGGTGGTACCAGGTGGGCATCATCAGC 761 50 QUERY: 1057 TGGGGAAAGAGCTGTGGA 1074 SBJCT: 762 TGGGGCAAGAGCTGTGGA 779

of 307 residues (94%) positive with, the 267 amino acid hypothetical protein [Macaca

fascicularis] (GenBank: AB046651) (SEQ ID NO:84) (Table 6G).

The FCTR6a amino acid has 247 of 267 amino acid residues (92%) identical to, and 251

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# Table 6G. BLASTP of FCTR6a and b against hypothetical protein [Macaca fascicularis] (SEQ ID NO:84)

	>GI   9651113   DBJ   BAB03569.1   (AB046651) HYPOTHETICAL PROTEIN [MACACA FASCICULARIS] LENGTH = 267
5	SCORE = 467 BITS (1202), EXPECT = E-131 IDENTITIES = 247/267 (92%), POSITIVES = 251/267 (94%)
10	QUERY: 1 MGFRFLGTANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILH 60
	QUERY: 61 KDFKRANMDNDIALLLLASPIKLDDLKVPICLPTQPGPATWRECWVAGWGQTNAADKNSV 120
15	SBJCT: 61 KDFKRANMDNDIALLLLASPITLDDLKVPICLPTQHGPATWHECWVAGWGQTNAADKNSV 120
20	QUERY: 121 KTDLMKVPMVIMDWEECSKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKWY 180
20	QUERY: 181 QVGIISWGKSCGDKNTPGIYTSLVNYNLWIEKVTQLGGRPFNAEKRRTSVKQKPMGSPVS 240
25	QUERY: 241 GVPEPGSPRSWLLLCPLSHVLFRAILY 267
30	K AND E ARE RESIDUES THAT DIFFER BETWEEN FCTR6A AND B. D193K, AND G217E.
;	The FCTR6a amino acid has 80 of 201 amino acid residues (39%) identical to, and 119
	of 201 residues (58%) positive with, the 638 amino acid plasma kallikrein B1 precursor
	(GENBANK-ID:NP_000883.1) (SEQ ID NO:85) (Table 6H).
35	(GENBANK-ID:NP_000883.1) (SEQ ID NO:85) (Table 6H).  Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID
35	
35	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID
35	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B
35	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B  PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO SAPIENS]
	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B  PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO SAPIENS]  GI   125184   SP   P03952   KAL HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN) (KININOGENIN)
	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B  PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO SAPIENS]  GI   125184   SP   P03952   KAL HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN)
40	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B  PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO SAPIENS]  GI   125184   SP   P03952   KAL HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN) (KININOGENIN)  (FLETCHER FACTOR)  GI   67591   PIR   KOHUP PLASMA KALLIKREIN (EC 3.4.21.34) PRECURSOR - HUMAN GI   190263   GB   AAA60153.1   (M13143) PLASMA PREKALLIKREIN [HOMO SAPIENS] GI   8809781   GB   AAAF79940.1   (AF232742) PLASMA KALLIKREIN PRECURSOR [HOMO SAPIENS]
40 45 50	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B  PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO SAPIENS]  GI   125184   SP   P03952   KAL HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN) (KININOGENIN)  (FLETCHER FACTOR)  GI   67591   PIR   KQHUP PLASMA KALLIKREIN (EC 3.4.21.34) PRECURSOR - HUMAN GI   190263   GB   AAA60153.1   (M13143) PLASMA PREKALLIKREIN [HOMO SAPIENS] GI   8809781   GB   AAF79940.1   (AF232742) PLASMA KALLIKREIN PRECURSOR [HOMO SAPIENS] LENGTH = 638  SCORE = 133 BITS (334), EXPECT = 3E-30
40	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B  PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO SAPIENS]  GI   125184   SP   P03952   KAL HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN) (KININOGENIN)  (FLETCHER FACTOR)  GI   67591   PIR   KOHUP PLASMA KALLIKREIN (EC 3.4.21.34) PRECURSOR - HUMAN GI   190263   GB   AAA60153.1   (M13143) PLASMA PREKALLIKREIN [HOMO SAPIENS] GI   8809781   GE   BAA79940.1   (AF232742) PLASMA KALLIKREIN PRECURSOR [HOMO SAPIENS] LENGTH = 638  SCORE = 133 BITS (334), EXPECT = 3E-30   IDENTITIES = 80/201 (39%), POSITIVES = 119/201 (58%), GAPS = 18/201 (8%)  QUERY: 20 LPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASILLHKDFKRANMDNDIALLLL 77       +   +   +   +           +   +
40 45 50	Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)  >GI   4504877   REF   NP_000883.1   PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA; KALLIKREIN B  PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO SAPIENS]  GI   125184   SP   P03952   KAL HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN) (KININOGENIN)  (FLETCHER FACTOR)  GI   67591   PIR   KOHUP PLASMA KALLIKREIN (EC 3.4.21.34) PRECURSOR - HUMAN GI   190263   GB   AAA60153.1   (M13143) PLASMA PREKALLIKREIN [HOMO SAPIENS] GI   8809781   GB   AAF79940.1   (AF232742) PLASMA KALLIKREIN PRECURSOR [HOMO SAPIENS] LENGTH = 638  SCORE = 133 BITS (334), EXPECT = 3E-30   IDENTITIES = 80/201 (39%), POSITIVES = 119/201 (58%), GAPS = 18/201 (8%)  QUERY: 20 LPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLL 77     +   +   +   +       +   +   +

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| | | | | | | | | | +
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                                                            | | | | | + | +
      SBJCT: 548 COKRYODYKITORMVCAGYKEGGKDACKGDSGGPLVC--KHNGMWRLVGITSWGEGCARR 605
      QUERY: 195 NTPGIYTSLVNYNLWIEKVTQ 215
5
                   ||+|| + | || + ||
      SBJCT: 606 EQPGVYTKVAEYMDWILEKTQ 626
      K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.
            The FCTR6a amino acid has 73 of 183 amino acid residues (39%) identical to, and 110
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      of 183 residues (59%) positive with, the 643 amino acid kallikrein [Sus scrofa] (GENBANK-
      ID:BAA37147.1) (SEQ ID NO:86) (Table 6I).
         Table 6I. BLASTP of FCTR6a and b against kallikrein [Sus scrofa] (SEQ ID NO:86)
      >GI | 4165315 | DBJ | BAA37147.1 | (AB022425) KALLIKREIN [SUS SCROFA]
15
                LENGTH = 643
       SCORE = 128 BITS (322), EXPECT = 9E-29
       IDENTITIES = 73/183 (39%), POSITIVES = 110/183 (59%), GAPS = 12/183 (6%)
20
               VLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLDDLKVPICLPTQ 95
                    +++ + + ++ |
                                      + +++
                                                   + | | | | + | +
      SBJCT: 459 ILNISEITKETPFSQVKE---IIIHQNYKILESGHDIALLKLETPLNYTDFQKPICLPSR 515
      QUERY: 96 PGP-ATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFP--KLTKNMLCAG 152
25
                                     |++| |+||
                       + ||| ||| |
      SBJCT: 516 DDTNVVYTNCWVTGWGFTE--EKGEIQNILQKVNIPLVSNEECQKSYRDHKISKQMICAG 573
      QUERY: 153 YKNESYDACKGDSGGPLVCTPEPGEKWYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEK 212
                       | | | | | | + | | | | | | | +
                                           |+ || ||+ | + ||+|| ++ | || +
      SBJCT: 574 YKEGGKDACKGESGGPLVC--KYNGIWHLVGTTSWGEGCARREQPGVYTKVIEYMDWILE 631
      QUERY: 213 VTQ 215
      SBJCT: 632 KTQ 634
35
      K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.
             The FCTR6a amino acid has 81 of 205 amino acid residues (39%) identical to, and 112
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      of 205 residues (54%) positive with, the 625 amino acid Coagulation factor XI [Homo sapiens]
      (embCAA64368.1) (SEQ ID NO:87) (Table 6J).
       Table 6J. BLASTP of FCTR6a and b against Coagulation factor XI [Homo sapiens] (SEQ
                                            ID NO:87)
      >GI | 180352 | GB | AAA51985.1 | (M20218) COAGULATION FACTOR XI [HOMO SAPIENS]
45
                LENGTH = 625
       SCORE = 127 BITS (320), EXPECT = 1E-28
       IDENTITIES = 81/205 (39%), POSITIVES = 112/205 (54%), GAPS = 17/205 (8%)
50
                 LPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKE-----VASIILHKDFKRANMDNDIA 73
      OUERY: 20
                            ||+|| ++
                                               | ||+| +| |
                   1 ++
      SBJCT: 427 LTAAHCFYGVESPKILRVYSGILNQS----EIKEDTSFFGVQEIIIHDQYKMAESGYDIA 482
      QUERY: 74 LLLLASPIKLDDLKVPICLPTQPG-PATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIM 132
55
                           + | | | | ++
                                                            + + | | | | | |
      SBJCT: 483 LLKLETTVNYTDSQRPICLPSKGDRNVIYTDCWVTGWGYRKLRDK--IQNTLQKAKIPLV 540
```

QUERY: 133 DWEECSKMFP--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKWYQVGIISWGKS 190

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The number of new cases of renal cell carcinoma in the United States in 1996 was projected to be 30,600 with an estimated 12,000 deaths. Tumors with a proposed histogenesis from the proximal tubule (clear-cell and chromophilic tumors) amount to 85% of renal cancers, whereas tumors with a proposed histogenesis from the connecting tubule/collecting duct (chromophobic-, oncocytic-, and duct Bellini-type tumors) amount to only 11%.

Adenocarcinomas may be separated into clear cell and granular cell carcinomas, although the 2 cell types may occur together in some tumors. The distinction between well-differentiated renal carcinomas and renal adenomas can be difficult. The diagnosis is usually made arbitrarily on the basis of size of the mass, but size alone should not influence the treatment approach, since metastases can occur with lesions as small as 0.5 centimeters.

While radical nephrectomy with regional lymphadenectomy, is the accepted, often curative therapy for stage I (localized disease) renal cell cancer, very little therapy is available for advance disease that represent about 70% of the patients. Radiotherapy as a postoperative adjuvant has not been effective, and when used preoperatively, may decrease local recurrence but does not appear to improve 5-yr survival. A chemotherapeutic agent capable of significantly altering the course of metastastic renal cell carcinoma has not been identified. (Renal Cell Cancer (PDQ®) Treatment - Health Professionals, Cancernet, NCI)

There is therefore a need to identify genes that are differentially modulated in renal-cell carcinomas. In addition there is a need for methods to assay candidate therapeutic substances for modulating expression of these genes. These substances might be recombinant protein expressed by the identified genes or antibodies that bind to the identified proteins. There is yet additionally a need for an effective method of identifying target molecules or related components. These and related needs and defects are addressed in the present invention.

### Novel kallikrein-like/coagulation factor XI-like Proteins and Nucleic Acids Encoding Same

FCTR6 is surprisingly found to be differentially expressed in clear cell Renal cell carcinoma tissues vs the normal adjacent kidney tissues. The present invention discloses a novel protein encoded by a cDNA and/or by genomic DNA and proteins similar to it, namely, new proteins bearing sequence similarity to kallikrein-like, nucleic acids that encode these proteins or

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fragments thereof, and antibodies that bind immunospecifically to a protein of the invention. It may have use as a therapeutic agent in the treatment of renal cancer and liver cirrhosis.

## The utility of kallikrein family members in protein therapy of Renal cancer

The treatment of renal cell carcinoma with recombinant kallikrein could improve disease outcome through several potential mechanisms. The literature suggests that members of this protein family are inhibitory to the process of angiogenesis, a process of vital importance to tumor progression. Renal cell carcinoma is known to be a highly angiogenic cancer. Thus, treatment of renal cell carcinoma with kallikrein may effectively shutdown the active recruitment of a blood supply to a tumor. Members of this protein family are known to play a role in vascular coagulation. Similar to anti-angiogenic therapy, a factor produced by cancer cells that is pro-coagulatory may also act to inhibit cancer growth by effectively "clogging" the tumor vascular supply. In addition, through its proteolytic activity, kallikrein may degrade ECM proteins or growth factors necessary for the progressive growth of cancer cells. Following is a relevant reference underlining the importance of Kallikrein in cancer therapy.

### The New Human Kallikrein Gene Family: Implications in Carcinogenesis.

Diamandis EP; Yousef GM; Luo I; Magklara I; Obiezu CV

Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada.

Trends Endocrinol Metab 2000 Mar;11(2):54-60.

ABSTRACT: The traditional human kallikrein gene family consists of three genes, namely KLK1 [encoding human kallikrein 1 (hK1) or pancreatic/renal kallikrein], KLK2 (encoding hK2, previously known as human glandular kallikrein 1) and KLK3 [encoding hK3 or prostate-specific antigen (PSA)]. KLK2 and KLK3 have important applications in prostate cancer diagnostics and, more recently, in breast cancer diagnostics. During

the past two to three years, new putative members of the human kallikrein gene family have been identified, including the PRSSL1 gene [encoding normal epithelial cell-specific 1 gene (NES1)], the gene encoding zyme/protease M/neurosin, the gene encoding prostase/KLK-L1, and the genes encoding neuropsin, stratum corneum chymotryptic enzyme and trypsin-like serine protease. Another five putative kallikrein genes, provisionally named KLK-L2, KLK-L3, KLK-L4, KLK-L5 and KLK-L6, have also been identified. Many of the newly identified kallikrein-like genes are regulated by steroid hormones, and a few kallikreins (NES1, protease M, PSA) are known to be downregulated in breast and possibly other cancers. NES1 appears to

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be a novel breast cancer tumor suppressor protein and PSA a potent inhibitor of angiogenesis. This brief review summarizes recent developments and possible applications of the newly defined and expanded human kallikrein gene locus.

# The utility of kallikrein-like/coagulation factor XI-like family members in protein therapy of liver cirrosis

Results related to inflammation shown below in Example A, Table CC3, panel 4, indicate over-expression of 27455183.0.19 in the liver cirrhosis sample, as compared to panel 1 data (Table CC1), where there is little or no expression in normal adult liver. Panel 4 was generated from various human cell lines that were untreated or resting as well as the same cells that were treated with a wide variety of immune modulatory molecules. There are several disease tissues represented as well as organ controls.

### Potential Role(s) of FCTR6 in Inflammation:

Liver cirrhosis occurs in patients with hepatitis C and also in alcoholics. This protein is 41% related to coagulation factor XI and its potential role in liver cirrhosis may be related to cleavage of kininogen. A reference for this follows:

Thromb Haemost 2000 May;83(5):709-14 High molecular weight kininogen is cleaved by FXIa at three sites: Arg409-Arg410, Lys502-Thr503 and Lys325-Lys326. Mauron T, Lammle B, Wuillemin WA Central Hematology Laboratory, University of Bern, Inselspital, Switzerland. Abstract:

We investigated the cleavage of high molecular weight kininogen (HK) by activated coagulation factor XI (FXIa) in vitro. Incubation of HK with FXIa resulted in the generation of cleavage products which were subjected to SDS-Page and analyzed by silverstaining, ligand-blotting and immunoblotting, respectively. Upon incubation with FXIa, bands were generated at 111, 100, 88 kDa on nonreduced and at 76, 62 and 51 kDa on reduced gels. Amino acid sequence analysis of the reaction mixtures revealed three cleavage sites at Arg409-Arg410, at Lys502-Thr503 and at Lys325-Lys326. Analysis of HK-samples incubated with FXIa for 3 min, 10 min and 120 min indicated HK to be cleaved first at Arg409-Arg410, followed by cleavage at Lys502-Thr503 and then at Lys325-Lys326. In conclusion, HK is cleaved by FXIa at three sites. Cleavage of HK by FXIa results in the loss of the surface binding site of HK, which may constitute a mechanism of inactivation of HK and of control of contact system activation.

### Impact of Therapeutic Targeting of FCTR6 in Inflammation:

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Therapeutic targeting of FCTR6 with a monoclonal antibody is anticipated to limit or block the extent of breakdown of kininogen and thereby reduce the degradation of liver that occurs in liver cirrhosis. A pertinent reference is:

Thromb Haemost 1999 Nov;82(5):1428-32 Parallel reduction of plasma levels of high and low molecular weight kiningen in patients with cirrhosis.

Cugno M, Scott CF, Salerno F, Lorenzano E, Muller-Esterl W, Agostoni A, Colman RW Department of Internal Medicine, IRCCS Maggiore Hospital, University of Milan, Italy. massimo.cugno@unimi.it

Abstract:

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Little is known about the regulation of high-molecular-weight-kininogen (HK) and lowmolecular-weight-kininogen (LK) or the relationship of each to the degree of liver function impairment in patients with cirrhosis. In this study, we evaluated HK and LK quantitatively by a recently described particle concentration fluorescence immunoassay (PCFIA) and qualitatively by SDS PAGE and immunoblotting analyses in plasma from 33 patients with cirrhosis presenting various degrees of impairment of liver function. Thirty-three healthy subjects served as normal controls. Patients with cirrhosis had significantly lower plasma levels of HK (median 49 microg/ml [range 22-99 microg/ml]) and LK (58 microg/ml [15-100 microg/ml]) than normal subjects (HK 83 microg/ml [65-115 microg/ml]; LK 80 microg/ml [45-120 microg/ml]) (p<0.0001). The plasma concentrations of HK and LK were directly related to plasma levels of cholinesterase (P<0.0001) and albumin (P<0.0001 and P<0.001) and inversely to the Child-Pugh score (P<0.0001) and to prothrombin time ratio (P<0.0001) (reflecting the clinical and laboratory abnormalities in liver disease). Similar to normal individuals, in patients with cirrhosis, plasma HK and LK levels paralleled one another, suggesting that a coordinate regulation of those proteins persists in liver disease. SDS PAGE and immunoblotting analyses of kininogens in cirrhotic plasma showed a pattern similar to that observed in normal controls for LK (a single band at 66 kDa) with some lower molecular weight forms noted in cirrhotic plasma. A slight increase of cleavage of HK (a major band at 130 kDa and a faint but increased band at 107 kDa) was evident. The increased cleavage of HK was confirmed by the lower cleaved kininogen index (CKI), as compared to normal controls. These data suggest a defect in hepatic synthesis as well as increased destructive cleavage of both kininogens in plasma from patients with cirrhosis. The decrease of important regulatory proteins like kininogens may contribute to the imbalance in coagulation and fibrinolytic systems, which frequently occurs in cirrhotic patients.

In summary, the differential expression of FCTR6 (Kallikrein family) in renal cell carcinoma is an important finding that could have immense potential in renal carcinogenesis. In

additon, overexpression of the above gene in liver cirrhosis demonstrates its anticipated use as an immunotherapeutic target.

### FCTR7

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The novel nucleic acid of 1498 nucleotides FCTR7 (also designated. 32592466.0.64) encoding a novel trypsin inhibitor-like protein is shown in Table 7A. An ORF begins with an ATG initiation codon at nucleotides 470-472 and ends with a TAA codon at nucleotides 1369-1371. Putative untranslated regions, if any, are found upstream from the initiation codon and downstream from the termination codon.

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GCGGCTGCAGAGGCCGGCCGTCCGGTTTGGCTCACCTCTCCCAGGAAACTTCACACTGGAGAGCCAAAAGGAGTGGAAGAGCCTGT  ${\tt CATGGCTAGAGCAATTCCAGCCATGGTTGCTTCCCAATGCCACTTTATTGGAGAAACTTTTTGGAAAAATACATGGATGAGGATGGTG}$ AGTGGTGGATAGCCAAACAACGAGGGAAAAGGGCCATCACAGACAATGACATGCAGAGTATTTTGGACCTTCATAATAAATTACGA AGTCAGGTGTATCCAACAGCCTCTAATATGGAGTATATGACATGGGATGTAGAGCTGGAAAGATCTGCAGAATCCAGGGCTGAAAT TGCTTGTGGGAACATGGACCTGCAAGCTTGCTTCCATCAATTGGACAGAATTTGGGAGCACACTGGGGAAGATATAGGCCCCCGAC  ${\tt GTTTCATGTACAATCGTGGTATGAAGTGAAAGACTTTAGCTACCCATATGAACATGAATGCAACCCATATTGTCCATTCAGGT}$ ATGAACATCTGGGGGCAGATATGGCCCAAAGCTGTCTACCTGGTGTGCAATTACTCCCCAAAGGGAAACTGGTGGGGGCCATGCCCC  ${\tt ACAGGTATTATCCCCCTCGAGAAGAGGAAACAAATGAAATAGAACGGCAGCAGTCACAAGTCCATGACACCCATGTCCGGACAAGA}$  ${\tt TCAGATGATAGTAGCAGAAATGAAGTCATTAGCTTTGGGAAAAGTAATGAAAATATAATGGTTTTAGAAATCCTGTGT{\tt TAA}{\tt A}{\tt TATT}$  $\underline{GCTATATTTTCTTAGCAGTTATTTCTACAGTTAATTACATAGTCATGATTGTTCTACGTTTCATATATTATATGGTGCTTTGTATA$ TGCCCCTAATAAAATGAATCTAAACATTGAAAAAA

The FCTR7 protein encoded by SEQ ID NO:24 has 300 amino acid residues and is presented using the one-letter code in Table 7B. The FCTR7 gene was found to be expressed in: brain; germ cell tumors. FCTR7 gene maps to Unigene cluster Hs.182364 which is expressed in the following tissues: brain, breast, ear, germ cell, heart, liver, lung, whole embryo, ovary, pancreas, pooled, prostate, stomach, testis, uterus, vascular. Therefore the FCTR7 protein described in this invention is also expressed in the above tissues.

The SignalP, Psort and/or Hydropathy profile for FCTR7 predict that this sequence has a signal peptide and is likely to be localized outside of the cell with a certainty of 0.4228. The SignalP shows a cleavage site between amino acids 20 and 21, *i.e.*, at the dash in the sequence amino acid ARA-IP. The predicted molecular weight of FCTR7 is 34739.9 Daltons. Hydropathy profile shows an amino terminal hydrophobic region. This region could function as a signal peptide and target the invention to be secreted or plasma membrane localized.

## Table 7B. Encoded FCTR7 protein sequence (SEQ ID NO:25).

MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDNDMQSILDLHNKLRSQVYPTASNMEYM TWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVV WATSNRIGCAINLCHNMNIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYKEGSDRYYPPREEETNE IERQQSQVHDTHVRTRSDDSSRNEVISFGKSNENIMVLEILC

This gene maps to Unigene cluster Hs.182364 which has been assigned the following mapping information shown in table 7C. Therefore the chromosomal assignment for this gene is the same as that for Unigene cluster 182364.

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### Table 7C. Mapping Information.

Chromosome:

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Gene Map 98:

Marker SHGC-32056, Interval D8S279-D8S526

Gene Map 98:

Marker SGC32056, Interval D8S526-D8S275

Gene Map 98:

Marker sts-G20223, Interval D8S526-D8S275

Gene Map 98:

Marker stSG30385, Interval D8S526-D8S275

Whitehead map:

EST67946, Chr.8

dbSTS entries:

G25853, G29349, G20223

The predicted amino acid sequence was searched in the publicly available GenBank database

FCTR7 protein showed Score = 743 (261.5 bits), Expect = 1.4e-73, P = 1.4e-73, 54 % identities (129 over 237 amino acids) and 43% homologies (167 over 237 amino acids) with human 25 kD trypsin inhibitor protein (258 aa; ACC:O43692) (Table 7D).

#### Table 7D. BLAST X search results are shown below:

20 ptnr:SPTREMBL-ACC:043692 25 KDA TRYPSIN INHIBITOR - HO... +2 743 8.4e-73 1 (SEQ ID NO:88)

ptnr:SPTREMBL-ACC:044228 HRTT-1 - HALOCYNTHIA RORETZI ... +2 325 2.9e-28 1 (SEQ ID NO:89)

ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED ... +2 314 5.3e-27 1 (SEQ ID NO:90)

ptnr:PIR-ID:JC4131 glioma pathogenesis-related protein... +2 309 2.0e-26 1 (SEQ ID NO:91)

ptnr:SWISSNEW-ACC:019010 CYSTEINE-RICH SECRETORY PROTE... +2 258 9.4e-21 1 (SEQ

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ID NO:92)

The nucleotide sequence of FCTR7 has 954 of 957 residues (99 %) identical to the 1-957 base segment, and 174 of 175 residues (99%) identical to bases 1317-1953 of the 2664

nucleotide Homo sapiens putative secretory protein precursor, mRNA (GenBank-ACC: AF142573) (SEQ ID NO:93) (Table 7E).

## Table 7E. BLASTN of FCTR7 against Putative secretory protein precursor (SEQ ID NO:93)

>qi|12002310|qb|AF142573.1|AF142573 Homo sapiens putative secretory protein 5 precursor, mRNA, complete cds Length = 2664Score = 1865 bits (941), Expect = 0.0 Identities = 954/957 (99%), Gaps = 1/957 (0%) 10 Strand = Plus / Plus Query: 364 gtccggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag 423 qtccggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag 60 15 Sbjct: 1 Query: 424 Sbjct: 61 20 gcgggagtggctcagagtaaccacagtgctgttcatggctagagcaattccagccatggt 543 Query: 484 gcgggagtggctcagagtaaccacagtgctgttcatggctagagcaattccagccatggt 180 Į. Sbjct: 121 fij ggttcccaatgccactttattggagaaacttttggaaaaatacatggatgaggatggtga 603 25 £25 Query: 544 ggttcccaatgccactttattggagaaacttttggaaaaatacatggatgaggatggtga 240 Sbjct: 181 i. L. gtggtggatagccaaacaacgagggaaaagggccatcacagacaatgacatgcagagtat 663 Query: 604 III 30 gtggtggatagccaaacaacgagggaaaagggccatcacagacaatgacatgcagagtat 300 Sbjct: 241 tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaatatggagta 723 Query: 664 tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaatatggagta 360 35 Sbjct: 301 tatgacatgggatgtagagctggaaagatctgcagaatccagggctgaaa-ttgcttgtg 782 Query: 724 tatgacatgggatgtagagctggaaagatctgcagaatcctgggctgaaagttgcttgtg 420 Sbjct: 361 40 ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 842 Query: 783 ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 480 Sbjct: 421 aagatataggcccccgacgtttcatgtacaatcgtggtatgatgaagtgaaagactttag 902 45 Query: 843 aagatataggcccccgacgtttcatgtacaatcgtggtatgatgaagtgaaagactttag 540 Sbjct: 481 ctacccatatgaacatgaatgcaacccatattgtccattcaggtgttctggccctgtatg 962 Query: 903 50 ctacccatatgaacatgaatgcaacccatattgtccattcaggtgttctggccctgtatg 600 Sbjct: 541 tacacattatacacaggtcgtgtgggcaactagtaacagaatcggttgtgccattaattt 1022 Query: 963 55 Sbjct: 601 tacacattatacacaggtcgtgtgggcaactagtaacagaatcggttgtgccattaattt 660 Query: 1023 gtgtcataacatgaacatctgggggcagatatggcccaaagctgtctacctggtgtgcaa 1082 Sbjct: 661 gtgtcataacatgaacatctgggggcagatatggcccaaagctgtctacctggtgtgcaa 720

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	Query: 1083 ttactccccaaagggaaactggtggggccatgccccttacaaacatgggcggccctgttc 1142
5	Query: 1143 tgcttgcccacctagttttggagggggctgtagagaaaatctgtgctacaaagaagggtc 1202
10	Sbjct: 781 tgcttgcccacctagttttggagggggctgtagagaaaatctgtgctacaaagaagggtc 840  Query: 1203 agacaggtattatcccctcgagaagaggaaacaaatgaaatagaacggcagcagtcaca 1262
15	Sbjct: 841 agacaggtattatcccctcgagaagaggaaacaaatgaaatagaacgacagcagtcaca 900  Query: 1263 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcat 1319
20	Score = 339 bits (171), Expect = 3e-90 Identities = 174/175 (99%) Strand = Plus / Plus
2.5	Query: 1317 cattagctttgggaaaagtaatgaaaatataatggttttagaaatcctgtgttaaatatt 1376
25 11 11 11 13 13	Query: 1377 gctatattttcttagcagttatttctacagttaattacatagtcatgattgttctacgtt 1436
Marie 1994 - 3 1 1994 - 3 1994	Query: 1437 tcatatattatatggtgctttgtatatgcccctaataaaatgaatctaaacattg 1491 
	The FCTR7 amino acid has 284 of 285 amino acid residues (99%) identical to, and 284
<b>≇</b> 2≅ 35	of 285 amino acid residues (99%) similar to, the 500 amino acid Putative secretory protein
ties, spreig spreig of H. W. West orde. Homb somb	precursor [Homo sapiens] (GenBank-Acc No.: AF142573) (SEQ ID NO:94) (Table 7F).
184	production [riomo suprema] (compound 1200 1.1.1.
	Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,
H. H	
f	Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,
Activity	Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,  (SEQ ID NO:94)  >gi   12002311   gb   AAG43287.1   AF142573 1 (AF142573) putative secretory protein precursor [Homo sapiens] Length = 500  Score = 581 bits (1499), Expect = e-165 Identities = 284/285 (99%), Positives = 284/285 (99%)
Lah	Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,  (SEQ ID NO:94)  >gi   12002311   gb   AAG43287.1   AF142573_1 (AF142573) putative secretory protein precursor [Homo sapiens] Length = 500  Score = 581 bits (1499), Expect = e-165
Lah	Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,  (SEQ ID NO:94)  >qi   12002311   qb   AAG43287.1   AF142573 1 (AF142573) putative secretory protein precursor [Homo sapiens] Length = 500  Score = 581 bits (1499), Expect = e-165 Identities = 284/285 (99%), Positives = 284/285 (99%)  Query: 1 MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDN 60
40	Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,  (SEQ ID NO:94)  > qi   12002311   gb   AAG43287.1   AF142573_1 (AF142573) putative secretory protein precursor [Homo sapiens] Length = 500  Score = 581 bits (1499), Expect = e-165 Identities = 284/285 (99%), Positives = 284/285 (99%)  Query: 1 MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDN 60

```
Sbjct: 181 CAINLCHNMNIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLC 240
       Query: 241 YKEGSDRYYPPREEETNEIERQQSQVHDTHVRTRSDDSSRNEVIS 285
                  5
       Sbjct: 241 YKEGSDRYYPPREEETNEIERQOSOVHDTHVRTRSDDSSRNEVIS 285
             The FCTR7 amino acid has 137 of 176 amino acid residues (78%) identical to, and 151
       of 176 amino acid residues (86%) similar to, the 188 amino acid Late gestation lung protein 1
       [Rattus norvegicus] (GenBank-Acc No.: AF109674) (SEQ ID NO:95) (Table 7G).
  10
        Table 7G. BLASTP alignments of FCTR7 against Late gestation lung protein 1, (SEQ ID
                                           NO:95)
       >gi|4324682|qb|AAD16986.1| (AF109674) late gestation lung protein 1 [Rattus
       norvegicus]
  15
                 Length = 188
        Score = 277 bits (709), Expect = 1e-73
        Identities = 137/176 (78%), Positives = 151/176 (86%)
                  LHNKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGONLGAHWGRY 127
  20
       Query: 68
                                                     1 25
                         LHNKLRGQVYPPASNMEYMTWDEELERSAAAWAQRCLWEHGPASLLVSIGQNLAVHWGRY 61
       Sbjct: 2
        Query: 128 RPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIGCAINLCH 187
                      RSPGFHVQSWYDEVKDYTYPYPHECNPWCPERCSGAMCTHYTQMVWATTNKIGCAVHTCR 121
       Sbict: 62
ļub
        Query: 188 NMNIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYKE 243
ij
                             Ti,
        Sbjct: 122 SMSVWGDIWENAVYLVCNYSPKGNWIGEAPYKHGRPCSECPSSYGGGCRNNLCYRE 177
  30
House many speed speed story. He is
              The FCTR7 amino acid has 130 of 237 amino acid residues (55%) identical to, and 165
        of 237 amino acid residues (70%) similar to, the 258 amino acid R3H domain-containing
        preproprotein; 25 kDa trypsin inhibitor [Homo sapiens] (GenBank-Acc No.: D45027) (SEQ ID
  35
        NO:96) (Table 7H).
         Table 7H. BLASTP alignments of FCTR7 against R3H domain-containing preproprotein,
                             25 kDa trypsin inhibitor (SEQ ID NO:96)
        >qi|7705676|ref|NP 056970.1| R3H domain-containing preproprotein; 25 kDa
  40
        trypsin inhibitor; R3H
                   domain (binds single-stranded nucleic acids) containing
                   [Homo sapiens]
         gi|2943716|dbj|BAA25066.1| (D45027) 25 kDa trypsin inhibitor [Homo sapiens]
                  Length = 258
  45
                  265 bits (678), Expect = 4e-70
         Identities = 130/237 (55%), Positives = 165/237 (70%), Gaps = 3/237 (1%)
                   TTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDNDMQSILDLHNK 71
        Query: 12
  50
                                   | + |
                                          +
                                                       | | | | + | | + | | +
                                              +
        Sbjct: 20 STVVLLNSTDSSPPTNNFTDIEAALKAQLDSAD---IPKARRKRYISQNDMIAILDYHNQ 76
```

	_		LRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRPPT 131 +
	Sbjct:	77	VRGKVFPPAANMEYMVWDENLAKSAEAWAATCIWDHGPSYLLRFLGQNLSVRTGRYRSIL 136
5	~ -		FHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIGCAINLCHNMNI 191  +          +++    +                   +
	Sbjct:	137	QLVKPWYDEVKDYAFPYPQDCNPRCPMRCFGPMCTHYTQMVWATSNRIGCAIHTCQNMNV 196
10	~ _		WGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYKEGSDRY 248
	Sbjct:	197	WGSVWRRAVYLVCNYAPKGNWIGEAPYKVGVPCSSCPPSYGGSCTDNLCFPGVTSNY 253

The FCTR7 amino acid has 109 of 233 amino acid residues (47%) identical to, and 146 of 233 amino acid residues (63%) similar to, the 253 amino acid Novel protein similar to a trypsin inhibitor [*Homo sapiens*] 25 kDa trypsin inhibitor (EMBLAcc No.: AL117382) (SEQ ID NO:97) (Table 7I).

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Table 7I. BLASTP alignments of FCTR7 against Novel protein similar to a trypsin inhibitor, (SEQ ID NO:97)

```
<u>ii</u>] 20
        >gi|9885193|emb|CAC04190.1| (AL117382) dJ881L22.3 (novel protein similar to a
111
        trypsin
Mark Core
                   inhibitor) [Homo sapiens]
                  Length = 253
25
                  225 bits (575), Expect = 4e-58
         Identities = 109/233 (47%), Positives = 146/233 (63%), Gaps = 8/233 (3%)
W
100
        Query: 10 RVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDNDMQSILDLH 69
                                                         + + | | | +
  30
                            1 11
                                    | + | +
Hart mad Kadi mad
                                                   --SGLEVPRYRRKRHISVRDMNALLDYH 70
                   QAVNALIMPNATPAPAQPESTAMRLL---
                   NKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRP 129
        Query: 70
                                                    |+| |||+ |+ +||||
                   | +|+ ||| |+||||| || || ||
                  NHIRASVYPPAANMEYMVWDKRLARAAEAWATQCIWAHGPSQLMRYVGQNLSIHSGQYRS 130
C) 35
        Query: 130 PTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIGCAINLCHNM 189
                                        ++|| +|
                                 + +
        Sbjct: 131 VVDLMKSWSEEKWHYLFPAPRDCNPHCPWRCDGPTCSHYTQMVWASSNRLGCAIHTCSSI 190
   40
        Query: 190 NIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYK 242
                         | +| |{|||+ |||| | +||| | +|||+|||+|||
        Sbjct: 191 SVWGNTWHRAAYLVCNYAIKGNWIGESPYKMGKPCSSCPPSYQGSCNSNMCFK 243
   45
```

The FCTR7 amino acid has 129 of 237 amino acid residues (54%) identical to, and 167 of 237 amino acid residues (70%) similar to, the 258 amino acid 25 kDa Trypsin Inhibitor from *Homo sapiens* (EMBLAcc No.: O43692) (SEQ ID NO:88) (Table 7J).

Table 7J. BLASTP alignments of FCTR7 against 25 kDa Trypsin Inhibitor, (SEQ ID NO:88)

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The FCTR7 amino acid has 79 of 193 amino acid residues (40%) identical to, and 110 of 193 amino acid residues (56%) similar to, the 266 amino acid Glioma Pathogenesis-Related Protein (RTVP-1 Protein) - *Homo sapiens* (SWISSPROT Acc No.: P48060) (SEQ ID NO:90) (Table 7K).

# Table 7K. BLASTP alignments of FCTR7 against Glioma Pathogenesis-Related Protein, (SEQ ID NO:90)

```
ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED PROTEIN (RTVP-1 PROTEIN)
- Homo sapiens (Human), 266 aa
Score = 314 (110.5 bits), Expect = 4.7e-28, P = 4.7e-28
Identities = 79/193 (40%), Positives = 110/193 (56%)
```

The FCTR7 amino acid has 66 of 186 amino acid residues (35%) identical to, and 91 of 186 amino acid residues (48%) similar to, the 186 amino acid Neutrophil granules matrix glycoprotein SGP28 precursor from *Homo sapiens* (SWISSPROT Acc No.: S68691) (SEQ ID NO:98) (Table 7L).

# Table 7L. BLASTP alignments of FCTR7 against Neutrophil granules matrix glycoprotein, (SEQ ID NO:98)

```
ptnr:PIR-ID:S68691 neutrophil granules matrix glycoprotein SGP28 precursor -
human
Score = 254 (89.4 bits), Expect = 1.1e-21, P = 1.1e-21
Identities = 66/186 (35%), Positives = 91/186 (48%)
```

A novel developmentally regulated gene with homology to a tumor derived trypsin inhibitor is expressed in lung mesenchyme, as described in Am. J. Physiol. 0:0-0(1999). cDNA cloning of a novel trypsin inhibitor with similarity to pathogenesis-related proteins, and its frequent expression in human brain cancer cells is disclosed in Biochim. Biophys. Acta 1395:202-208(1998). RTVP-1, a novel human gene with sequence similarity to genes of diverse species, is expressed in tumor cell lines of glial but not neuronal origin, as published in Gene 180:125-130(1996). The human glioma pathogenesis-related protein is structurally related to plan pathogenesis-related proteins and its gene is expressed specifically in brain tumors (Gene 159:131-135(1995)). Structure comparison of human glioma pathogenesis-related protein GliPR and the plant pathogenesis-related protein P14a indicates a functional link between the human

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immune system and a plant defense system (Proc. Natl. Acad. Sci. U.S.A. 95:2262-2266(1998)). GliPR is highly expressed in the human brain tumor, glioblastoma multiform/astrocytome, but neither in normal fetal or adult brain tissue, nor in other nervous system tumors. GliPR belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1. SGP28, a novel matrix glycoprotein in specific granules of human neutrophils with similarity to a human testis-specific gene product and to a rodent sperm-coating glycoprotein (FEBS Lett. 380, 246-250, 1996). The primary structure and properties of helothermine, a peptide toxin that blocks ryanodine receptors is described in Biophys. J. 68:2280-2288(1995). As GliPR, Helothermine belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1.

Based upon homology, FCTR7 protein and each homologous protein or peptide may share at least some activity.

### Therapeutic uses:

FCTR7 protein has homology to trypsin inhibitors, Q91055 helothermine, tumor derived tyrpsin inhibitors, glioma pathogenesis-related protein, Q9Z0U6 LATE GESTATION LUNG PROTEIN 1, and to the Prosite family which groups mammalian SCP/TPX1;INSECTS AG3/AG5; FUNGI SC7/SC14 AND PLANTS PR-1 proteins. Therefore the FCTR7 protein disclosed in this invention could function like the proteins which it has homology to. These functions include tissue development in vitro and in vivo, and cancer pathogenesis.

Based the tissue expression pattern, the gene is implicated in diseases of tissues in which it is expressed. These diseases include but are not limited to:

- Glioma,
- cancer,
- 25 lung diseases,
  - gestation,
  - male and female reproductive diseases,
  - deafness,
  - neurological disorders,
- gastric disorders, and 30
  - pancreatic diseases like diabetes.

These materials are further useful in the generation of antibodies that bind immunospecifically to the novel FCTR7 substances for use in therapeutic or diagnostic methods.

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These antibodies may be generated according to methods known in the art, using prediction from hydrophobicity charts, as described in the "Anti-FCTRX Antibodies" section below. In one embodiment, a contemplated FCTR7 epitope is from aa 40 to 120. In another embodiment, a FCTR7 epitope is from aa 130 to 170. In additional embodiments, FCTR7 epitopes are from aa 210 to 230, and from aa 240 to 280.

TABLE 8A: Summary Of Nucleic Acids And Proteins Of The Invention

Name Tables		Clone; Description of Homolog	Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	
FCTR1	1A, 1B,	58092213.0.36 follistatin-like protein	1	2	
FCTR2	2A, 2B	AC012614_1.0.123; KIAA1061-like protein	3	4	
		10129612.0.118; neurestin-like protein	5	6	
	3C, 3D 10129612.0.405; neurestin-like protein		7	8	
	3E 10129612.0.154; neurestin-like protein		9		
	3F 10129612.0.67; neurestin-like protein		10		
	3G 10129612.0.258; neurestin-like protein		11		
	3H, 3I	10129612.0.352; neurestin-like protein	12	13	
FCTR4	4A, 4B	29692275.0.1; NF-Kappa-B P65delta3-like	14	15	
		protein			
FCTR5	5A, 5B	32125243.0.21; human complement C1R	16	17	
		component precursor -like protein			
	5C, 5D		18	19	
FCTR6	6A, 6B	27455183.0.19; novel human blood	20	21	
		coagulation factor XI -like protein			
	6C, 6D	27455183.0.145; novel human blood	22	23	
		coagulation factor XI -like protein			
FCTR7	7A, 7B	32592466.0.64; trypsin inhibitor -like protein	24	25	
FCTR1	Example 2	Ag809 Forward	26		
FCTR1	Example 2	Ag809 Probe	27		
FCTR1	Example 2	Ag809 Reverse	28		
FCTR4	Example 2	Ag2773 Forward	29		
FCTR4	Example 2	Ag2773 Probe	30		
FCTR4	Example 2	Ag2773 Reverse	31		
FCTR5	Example 2	Ag427 Forward	32		
FCTR5	Example 2	Ag427 Probe	33		
FCTR5	Example 2	Ag427 Reverse	34		
FCTR6	Example 2	Ag1541 Forward	35		
FCTR6	Example 2	Ag1541 Probe	36		
FCTR6	Example 2	Ag1541 Reverse	37		

TABLE 8B: Summary of Query Sequences Disclosed

Table	Database	Acc. No.	Sequence Name	Species	SEQ ID NO.
1C, 1K	remtrEmbl	BAA21725	IGFBP-like protein	mouse	38
1D	sptrEmbl	Q61581	Follistatin-like protein-2	Mouse	39

E	SptrEmbl		Mac23 process		40
F, 1K	SptrEmbl		IVIAO23 protein		41
G, 1K	SptrEmbl	Q16270	1 Tostacy of the Stemana Barrers		42
H, 1K		B40098	Colorectal cancer suppressor		43
Ī	TrEmblne w	AAD9360	PTP sigma (brain) precursor	Human	44
J	SptrEmbl	Q13332	PTP sigma precursor	Human	45
i.C	GenBank		KIAA1061 cDNA	Human	46
D	TrEmblne w	BAA85677	KIAA1263	Human	47
EΕ	TrEmblne w	BAA83013	KIAA1061 protein fragment	Human	48
F	Embl	CAB70877.1	Hypothetical protein DKFzp566D234.1	Human	49
2G	GenBank	Q62632	Follistatin-related protein-1 precursor	Rat	50
2H	GenBank	Q62536	Follistatin-related protein-1 precursor	Mouse	51
2I	GenBank	JG0187	Follistatin related protein	African clawed frog	52
2J	GenBank	Q12841	Follistatin related protein-1 precursor	Human	53
2K	Embl	CAB42968.1	Flik protein	Chicken	54
 2L	GenBank	T13822	Frazzled gene protein	Fruit fly	55
2M	GenBank	AAC38849.1	Roundabout 1	Fruit fly	56
2N	GenBank	O60469	Down Syndrome Cell Adhesion Molecule Precursor	Human`	57
20	SwissProt	Q13449	Limbic system-associated membrane protein precursor	Human	58
2P	SptrEmbl	O70246	Putative neuronal cell adhesion molecule, short form	Mouse	59
2Q	SptrEmbl	O02869	CHLAMP, G11-isoform precursor	Chicken	60
2R	SwissProt	Q62813	Limbic system-associated membrane protein precursor	Rat	61
3J	GenBank	NM 011856.2	Odd Oz/ten-m homology 2	Fruit fly	62
3K	Embl	AJ245711.1	Teneurin-2 cDNA, short splice variant	Chicken	63
3L	GenBank	AB032953	KIAA 1127 cDNA	Human	64
3M, 3U	GenBank	AB025411	Ten-m2 cDNA	Mouse	65
3N	GenBank	NM_020088.1	Neurestin alpha cDNA	Rat	66
30	Embl	GGA278031	Teneurin-2	Chicken	67
3P	GenBank	NP_035986.2	Odd Oz/ten-m homology 2	Fruit fly	68
3Q	Embl	CAC09416.1	Teneurin-2	Chicken	69
3R	GenBank	BAA77399.1	Ten-m4	Mouse	70
3S	GenBank	AB032953	KIAA1127 protein	Human	71
3T	GenBank	AF086607	Neurestin alpha	Rat	72
4C	SptrEmbl	Q99233	Hypothetical 10 kD protein	Trypanos ome	
4C	SptrEmbl	Q16896	GABA receptor subunit		74
4C	SptrEmbl	O76473	GABA receptor subunit		75
4C	TrEmblne w		FI3J11.13 protein		76

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Text p. 90	SptrEmbl	Q13313	NF-kappa B P65 delta 3 protein	Human	77
5E	GenBank	XM_007061.1	Complement C1R-like proteinase precursor	Human	78
5F	GenBank	NM_001733.1	Complement component 1, R subcomponent cDNA	Human	79
5G	GenBank	AAF44349.1	Complement C1R-like proteinase precursor	Human	80
5H	GenBank	AAA5185.1	Complement C1R component precursor	Human	81
6E	GenBank	AB046651	Brain cDNA clone Qcc-17034	Macaque	82
6F	GenBank	AK09660	Adult testis cDNA, RIKEN full length enriched	Mouse	83
6G	GenBank	AB046651	Hypothetical protein	Macaque	84
6H	GenBank	NP_000838.1	Plasma kallikrein B1 precursor	Human	85
6I	GenBank	BAA37147.1	Kallikrein	Pig	86
6J	Embl	CAA64368.1	Coagulation factor XI	Human	87
7D, 7J	SptrEmbl	O43692	25 kDa trypsin inhibitor	Human	88
7D	SptrEmbl	O44228	HRTT-1		89
7D, 7K	SptrEmbl	P418060	Glioma pathogenesis-related protein	Human	90
7D	PIR-ID	JC4131	Glioma pathogenesis-related protein	Human	91
7D	SwissProt	O19010	Cysteine-rcih secretory protein		92
7E	GenBank	AF142573	Putatitive secretory protein precursor cDNA	Human	93
7F	GenBank	AF142573	Putative secretory protein precursor	Human	94
7G	GenBank	AF109674	Late gestation lung protein 1	Rat	95
7H	GenBank	D45027	R3H domain containing preprotein, 25 kDa trypsin inhibitor	Human	96
7I	Embl	AL117382	Novel protein similar to a trypsin inhibitor	Human	97
7L	PIR-ID	S68691	Neutrophil granules matrix glycoprotein SGP28 precursor	Human	98

### **FCTRX** Nucleic Acids and Polypeptides

One aspect of the invention pertains to isolated nucleic acid molecules that encode FCTRX polypeptides or biologically-active portions thereof. Also included in the invention are nucleic acid fragments sufficient for use as hybridization probes to identify FCTRX-encoding nucleic acids (*e.g.*, FCTRX mRNAs) and fragments for use as PCR primers for the amplification and/or mutation of FCTRX nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs, and derivatives, fragments and homologs thereof. The nucleic acid molecule may be single-stranded or double-stranded, but preferably is comprised double-stranded DNA.

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An FCTRX nucleic acid can encode a mature FCTRX polypeptide. As used herein, a "mature" form of a polypeptide or protein disclosed in the present invention is the product of a naturally occurring polypeptide or precursor form or proprotein. The naturally occurring polypeptide, precursor or proprotein includes, by way of nonlimiting example, the full length gene product, encoded by the corresponding gene. Alternatively, it may be defined as the polypeptide, precursor or proprotein encoded by an ORF described herein. The product "mature" form arises, again by way of nonlimiting example, as a result of one or more naturally occurring processing steps as they may take place within the cell, or host cell, in which the gene product arises. Examples of such processing steps leading to a "mature" form of a polypeptide or protein include the cleavage of the N-terminal methionine residue encoded by the initiation codon of an ORF, or the proteolytic cleavage of a signal peptide or leader sequence. Thus a mature form arising from a precursor polypeptide or protein that has residues 1 to N, where residue 1 is the N-terminal methionine, would have residues 2 through N remaining after removal of the N-terminal methionine. Alternatively, a mature form arising from a precursor polypeptide or protein having residues 1 to N, in which an N-terminal signal sequence from residue 1 to residue M is cleaved, would have the residues from residue M+1 to residue N remaining. Further as used herein, a "mature" form of a polypeptide or protein may arise from a step of post-translational modification other than a proteolytic cleavage event. Such additional processes include, by way of non-limiting example, glycosylation, myristoylation or phosphorylation. In general, a mature polypeptide or protein may result from the operation of only one of these processes, or a combination of any of them.

The term "probes", as utilized herein, refers to nucleic acid sequences of variable length, preferably between at least about 10 nucleotides (nt), 100 nt, or as many as approximately, e.g., 6,000 nt, depending upon the specific use. Probes are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are generally obtained from a natural or recombinant source, are highly specific, and much slower to hybridize than shorter-length oligomer probes. Probes may be single- or double-stranded and designed to have specificity in PCR, membrane-based hybridization technologies, or ELISA-like technologies.

The term "isolated" nucleic acid molecule, as utilized herein, is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5'- and 3'-termini of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated FCTRX nucleic acid molecules can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb,

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0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell/tissue from which the nucleic acid is derived (e.g., brain, heart, liver, spleen, etc.). Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material or culture medium when produced by recombinant techniques, or of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement of this aforementioned nucleotide sequence, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24 as a hybridization probe, FCTRX molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, *et al.*, (eds.), MOLECULAR CLONING: A LABORATORY MANUAL 2<sup>nd</sup> Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989; and Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993.)

A nucleic acid of the invention can be amplified using cDNA, mRNA or alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to FCTRX nucleotide sequences can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

As used herein, the term "oligonucleotide" refers to a series of linked nucleotide residues, which oligonucleotide has a sufficient number of nucleotide bases to be used in a PCR reaction. A short oligonucleotide sequence may be based on, or designed from, a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue. Oligonucleotides comprise portions of a nucleic acid sequence having about 10 nt, 50 nt, or 100 nt in length, preferably about 15 nt to 30 nt in length. In one embodiment of the invention, an oligonucleotide comprising a nucleic acid molecule less than 100 nt in length would further comprise at least 6 contiguous nucleotides of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement thereof. Oligonucleotides may be chemically synthesized and may also be used as probes.

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion of this nucleotide sequence (e.g., a

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fragment that can be used as a probe or primer or a fragment encoding a biologically-active portion of an FCTRX polypeptide). A nucleic acid molecule that is complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, is one that is sufficiently complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that it can hydrogen bond with little or no mismatches to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby forming a stable duplex.

As used herein, the term "complementary" refers to Watson-Crick or Hoogsteen base pairing between nucleotides units of a nucleic acid molecule, and the term "binding" means the physical or chemical interaction between two polypeptides or compounds or associated polypeptides or compounds or combinations thereof. Binding includes ionic, non-ionic, van der Waals, hydrophobic interactions, and the like. A physical interaction can be either direct or indirect. Indirect interactions may be through or due to the effects of another polypeptide or compound. Direct binding refers to interactions that do not take place through, or due to, the effect of another polypeptide or compound, but instead are without other substantial chemical intermediates.

Fragments provided herein are defined as sequences of at least 6 (contiguous) nucleic acids or at least 4 (contiguous) amino acids, a length sufficient to allow for specific hybridization in the case of nucleic acids or for specific recognition of an epitope in the case of amino acids, respectively, and are at most some portion less than a full length sequence. Fragments may be derived from any contiguous portion of a nucleic acid or amino acid sequence of choice. Derivatives are nucleic acid sequences or amino acid sequences formed from the native compounds either directly or by modification or partial substitution. Analogs are nucleic acid sequences or amino acid sequences that have a structure similar to, but not identical to, the native compound but differs from it in respect to certain components or side chains. Analogs may be synthetic or from a different evolutionary origin and may have a similar or opposite metabolic activity compared to wild type. Homologs are nucleic acid sequences or amino acid sequences of a particular gene that are derived from different species.

Derivatives and analogs may be full length or other than full length, if the derivative or analog contains a modified nucleic acid or amino acid, as described below. Derivatives or analogs of the nucleic acids or proteins of the invention include, but are not limited to, molecules comprising regions that are substantially homologous to the nucleic acids or proteins of the invention, in various embodiments, by at least about 70%, 80%, or 95% identity (with a preferred identity of 80-95%) over a nucleic acid or amino acid sequence of identical size or

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when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to the complement of a sequence encoding the aforementioned proteins under stringent, moderately stringent, or low stringent conditions. See *e.g.* Ausubel, *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993, and below.

A "homologous nucleic acid sequence" or "homologous amino acid sequence," or variations thereof, refer to sequences characterized by a homology at the nucleotide level or amino acid level as discussed above. Homologous nucleotide sequences encode those sequences coding for isoforms of FCTRX polypeptides. Isoforms can be expressed in different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. In the invention, homologous nucleotide sequences include nucleotide sequences encoding for an FCTRX polypeptide of species other than humans, including, but not limited to: vertebrates, and thus can include, *e.g.*, frog, mouse, rat, rabbit, dog, cat cow, horse, and other organisms. Homologous nucleotide sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous nucleotide sequence does not, however, include the exact nucleotide sequence encoding human FCTRX protein. Homologous nucleic acid sequences include those nucleic acid sequences that encode conservative amino acid substitutions (see below) in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, as well as a polypeptide possessing FCTRX biological activity. Various biological activities of the FCTRX proteins are described below.

An FCTRX polypeptide is encoded by the open reading frame ("ORF") of an FCTRX nucleic acid. An ORF corresponds to a nucleotide sequence that could potentially be translated into a polypeptide. A stretch of nucleic acids comprising an ORF is uninterrupted by a stop codon. An ORF that represents the coding sequence for a full protein begins with an ATG "start" codon and terminates with one of the three "stop" codons, namely, TAA, TAG, or TGA. For the purposes of this invention, an ORF may be any part of a coding sequence, with or without a start codon, a stop codon, or both. For an ORF to be considered as a good candidate for coding for a *bona fide* cellular protein, a minimum size requirement is often set, *e.g.*, a stretch of DNA that would encode a protein of 50 amino acids or more.

The nucleotide sequences determined from the cloning of the human FCTRX genes allows for the generation of probes and primers designed for use in identifying and/or cloning FCTRX homologues in other cell types, e.g. from other tissues, as well as FCTRX homologues from other vertebrates. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that

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hybridizes under stringent conditions to at least about 12, 25, 50, 100, 150, 200, 250, 300, 350 or 400 consecutive sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or an anti-sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or of a naturally occurring mutant of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Probes based on the human FCTRX nucleotide sequences can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In various embodiments, the probe further comprises a label group attached thereto, *e.g.* the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express an FCTRX protein, such as by measuring a level of an FCTRX-encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting FCTRX mRNA levels or determining whether a genomic FCTRX gene has been mutated or deleted.

"A polypeptide having a biologically-active portion of an FCTRX polypeptide" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. A nucleic acid fragment encoding a "biologically-active portion of FCTRX" can be prepared by isolating a portion of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that encodes a polypeptide having an FCTRX biological activity (the biological activities of the FCTRX proteins are described below), expressing the encoded portion of FCTRX protein (e.g., by recombinant expression *in vitro*) and assessing the activity of the encoded portion of FCTRX.

#### FCTRX Nucleic Acid and Polypeptide Variants

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, due to degeneracy of the genetic code and thus encode the same FCTRX proteins as that encoded by the nucleotide sequences shown in SEQ ID NO NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

In addition to the human FCTRX nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the FCTRX

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polypeptides may exist within a population (e.g., the human population). Such genetic polymorphism in the FCTRX genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame (ORF) encoding an FCTRX protein, preferably a vertebrate FCTRX protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the FCTRX genes. Any and all such nucleotide variations and resulting amino acid polymorphisms in the FCTRX polypeptides, which are the result of natural allelic variation and that do not alter the functional activity of the FCTRX polypeptides, are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding FCTRX proteins from other species, and thus that have a nucleotide sequence that differs from the human sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the FCTRX cDNAs of the invention can be isolated based on their homology to the human FCTRX nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 6 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, the nucleic acid is at least 10, 25, 50, 100, 250, 500, 750, 1000, 1500, or 2000 or more nucleotides in length. In yet another embodiment, an isolated nucleic acid molecule of the invention hybridizes to the coding region. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other.

Homologs (*i.e.*, nucleic acids encoding FCTRX proteins derived from species other than human) or other related sequences (*e.g.*, paralogs) can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular human sequence as a probe using methods well known in the art for nucleic acid hybridization and cloning.

As used herein, the phrase "stringent hybridization conditions" refers to conditions under which a probe, primer or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures than shorter sequences. Generally, stringent conditions are selected to be about 5°C lower than the thermal

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melting point (Tm) for the specific sequence at a defined ionic strength and pH. The Tm is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present at excess, at Tm, 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (e.g., 10 nt to 50 nt) and at least about 60°C for longer probes, primers and oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

Stringent conditions are known to those skilled in the art and can be found in Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Preferably, the conditions are such that sequences at least about 65%, 70%, 75%, 85%, 90%, 95%, 98%, or 99% homologous to each other typically remain hybridized to each other. A non-limiting example of stringent hybridization conditions are hybridization in a high salt buffer comprising 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm DNA at 65°C, followed by one or more washes in 0.2X SSC, 0.01% BSA at 50°C. An isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (*e.g.*, encodes a natural protein).

In a second embodiment, a nucleic acid sequence that is hybridizable to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of moderate stringency is provided. A non-limiting example of moderate stringency hybridization conditions are hybridization in 6X SSC, 5X Denhardt's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA at 55°C, followed by one or more washes in 1X SSC, 0.1% SDS at 37°C. Other conditions of moderate stringency that may be used are well-known within the art. See, e.g., Ausubel, et al. (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990; GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY.

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In a third embodiment, a nucleic acid that is hybridizable to the nucleic acid molecule comprising the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of low stringency, is provided. A non-limiting example of low stringency hybridization conditions are hybridization in 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml denatured salmon sperm DNA, 10% (wt/vol) dextran sulfate at 40°C, followed by one or more washes in 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS at 50°C. Other conditions of low stringency that may be used are well known in the art (e.g., as employed for cross-species hybridizations). See, e.g., Ausubel, et al. (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990, GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY; Shilo and Weinberg, 1981. *Proc Natl Acad Sci USA* 78: 6789-6792.

#### Conservative Mutations

In addition to naturally-occurring allelic variants of FCTRX sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby leading to changes in the amino acid sequences of the encoded FCTRX proteins, without altering the functional ability of said FCTRX proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequences of the FCTRX proteins without altering their biological activity, whereas an "essential" amino acid residue is required for such biological activity. For example, amino acid residues that are conserved among the FCTRX proteins of the invention are predicted to be particularly non-amenable to alteration. Amino acids for which conservative substitutions can be made are well-known within the art.

Another aspect of the invention pertains to nucleic acid molecules encoding FCTRX proteins that contain changes in amino acid residues that are not essential for activity. Such FCTRX proteins differ in amino acid sequence from SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet retain biological activity. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 45% homologous to the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. Preferably, the protein encoded by the nucleic acid molecule is at least about 60% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; more

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preferably at least about 70% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; still more preferably at least about 80% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; even more preferably at least about 90% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; and most preferably at least about 95% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

An isolated nucleic acid molecule encoding an FCTRX protein homologous to the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein.

Mutations can be introduced into SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted, non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined within the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted non-essential amino acid residue in the FCTRX protein is replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an FCTRX coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for FCTRX biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, the encoded protein can be expressed by any recombinant technology known in the art and the activity of the protein can be determined.

The relatedness of amino acid families may also be determined based on side chain interactions. Substituted amino acids may be fully conserved "strong" residues or fully conserved "weak" residues. The "strong" group of conserved amino acid residues may be any one of the following groups: STA, NEQK, NHQK, NDEQ, QHRK, MILV, MILF, HY, FYW, wherein the single letter amino acid codes are grouped by those amino acids that may be substituted for each other. Likewise, the "weak" group of conserved residues may be any one of

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the following: CSA, ATV, SAG, STNK, STPA, SGND, SNDEQK, NDEQHK, NEQHRK, VLIM, HFY, wherein the letters within each group represent the single letter amino acid code.

In one embodiment, a mutant FCTRX protein can be assayed for (i) the ability to form protein:protein interactions with other FCTRX proteins, other cell-surface proteins, or biologically-active portions thereof, (ii) complex formation between a mutant FCTRX protein and an FCTRX ligand; or (iii) the ability of a mutant FCTRX protein to bind to an intracellular target protein or biologically-active portion thereof; (e.g. avidin proteins).

In yet another embodiment, a mutant FCTRX protein can be assayed for the ability to regulate a specific biological function (e.g., regulation of insulin release).

### **Antisense Nucleic Acids**

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein (*e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence). In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire FCTRX coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of an FCTRX protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; or antisense nucleic acids complementary to an FCTRX nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an FCTRX protein. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding the FCTRX protein. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding the FCTRX protein disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and

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Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of FCTRX mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of FCTRX mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of FCTRX mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally-occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids (e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used).

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated in situ such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding an FCTRX protein to thereby inhibit expression of the protein (e.g., by inhibiting transcription and/or translation). The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the

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double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface (e.g., by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens). The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient nucleic acid molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other. See, *e.g.*, Gaultier, *et al.*, 1987. *Nucl. Acids Res.* 15: 6625-6641. The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (see, *e.g.*, Inoue, *et al.* 1987. *Nucl. Acids Res.* 15: 6131-6148) or a chimeric RNA-DNA analogue (see, *e.g.*, Inoue, *et al.*, 1987. *FEBS Lett.* 215: 327-330.

### Ribozymes and PNA Moieties

Nucleic acid modifications include, by way of non-limiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject.

In one embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes as described in Haselhoff and Gerlach 1988. *Nature* 334: 585-591) can be used to catalytically cleave FCTRX mRNA transcripts to thereby inhibit translation of FCTRX mRNA. A ribozyme having specificity for an FCTRX-encoding nucleic acid can be designed based upon the nucleotide sequence of an FCTRX cDNA disclosed herein (*i.e.*, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an FCTRX-encoding mRNA. See, *e.g.*, U.S. Patent 4,987,071 to Cech, *et al.* and U.S. Patent

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5,116,742 to Cech, *et al.* FCTRX mRNA can also be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, FCTRX gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the FCTRX nucleic acid (*e.g.*, the FCTRX promoter and/or enhancers) to form triple helical structures that prevent transcription of the FCTRX gene in target cells. *See, e.g.*, Helene, 1991. *Anticancer Drug Des.* 6: 569-84; Helene, *et al.* 1992. *Ann. N.Y. Acad. Sci.* 660: 27-36; Maher, 1992. *Bioassays* 14: 807-15.

In various embodiments, the FCTRX nucleic acids can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids. *See*, *e.g.*, Hyrup, *et al.*, 1996. *Bioorg Med Chem 4*: 5-23. As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics (*e.g.*, DNA mimics) in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup, *et al.*, 1996. *supra*; Perry-O'Keefe, *et al.*, 1996. *Proc. Natl. Acad. Sci. USA* 93: 14670-14675.

PNAs of FCTRX can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of FCTRX can also be used, for example, in the analysis of single base pair mutations in a gene (e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S<sub>1</sub> nucleases (see, Hyrup, et al., 1996.supra); or as probes or primers for DNA sequence and hybridization (see, Hyrup, et al., 1996, supra; Perry-O'Keefe, et al., 1996. supra).

In another embodiment, PNAs of FCTRX can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of FCTRX can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes (*e.g.*, RNase H and DNA polymerases) to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using

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linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (*see*, Hyrup, etal., 1996. *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup, *et al.*, 1996. *supra* and Finn, *et al.*, 1996. *Nucl Acids Res* 24: 3357-3363. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA. *See*, *e.g.*, Mag, *et al.*, 1989. *Nucl Acid Res* 17: 5973-5988. PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment. *See*, *e.g.*, Finn, *et al.*, 1996. *supra*. Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. *See*, *e.g.*, Petersen, *et al.*, 1975. *Bioorg. Med. Chem. Lett.* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (*see*, *e.g.*, Letsinger, *et al.*, 1989. *Proc. Natl. Acad. Sci. U.S.A.* 86: 6553-6556; Lemaitre, *et al.*, 1987. *Proc. Natl. Acad. Sci.* 84: 648-652; PCT Publication No. WO88/09810) or the blood-brain barrier (*see*, *e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (*see*, *e.g.*, Krol, *et al.*, 1988. *BioTechniques* 6:958-976) or intercalating agents (*see*, *e.g.*, Zon, 1988. *Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, and the like.

### **FCTRX Polypeptides**

A polypeptide according to the invention includes a polypeptide including the amino acid sequence of FCTRX polypeptides whose sequences are provided in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residues shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, while still encoding a protein that maintains its FCTRX activities and physiological functions, or a functional fragment thereof.

In general, an FCTRX variant that preserves FCTRX-like function includes any variant in which residues at a particular position in the sequence have been substituted by other amino acids, and further include the possibility of inserting an additional residue or residues between two residues of the parent protein as well as the possibility of deleting one or more residues from the parent sequence. Any amino acid substitution, insertion, or deletion is encompassed by the

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invention. In favorable circumstances, the substitution is a conservative substitution as defined above.

One aspect of the invention pertains to isolated FCTRX proteins, and biologically-active portions thereof, or derivatives, fragments, analogs or homologs thereof. Also provided are polypeptide fragments suitable for use as immunogens to raise anti-FCTRX antibodies. In one embodiment, native FCTRX proteins can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, FCTRX proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, an FCTRX protein or polypeptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the FCTRX protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of FCTRX proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the language "substantially free of cellular material" includes preparations of FCTRX proteins having less than about 30% (by dry weight) of non-FCTRX proteins (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-FCTRX proteins, still more preferably less than about 10% of non-FCTRX proteins, and most preferably less than about 5% of non-FCTRX proteins. When the FCTRX protein or biologically-active portion thereof is recombinantly-produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the FCTRX protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of FCTRX proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of FCTRX proteins having less than about 30% (by dry weight) of chemical precursors or non-FCTRX chemicals, more preferably less than about 20% chemical precursors or non-FCTRX chemicals, still more preferably less than about 10% chemical precursors or non-FCTRX chemicals, and most preferably less than about 5% chemical precursors or non-FCTRX chemicals.

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Biologically-active portions of FCTRX proteins include peptides comprising amino acid sequences sufficiently homologous to or derived from the amino acid sequences of the FCTRX proteins (e.g., the amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25) that include fewer amino acids than the full-length FCTRX proteins, and exhibit at least one activity of an FCTRX protein. Typically, biologically-active portions comprise a domain or motif with at least one activity of the FCTRX protein. A biologically-active portion of an FCTRX protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acid residues in length.

Moreover, other biologically-active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native FCTRX protein.

In an embodiment, the FCTRX protein has an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. In other embodiments, the FCTRX protein is substantially homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail, below. Accordingly, in another embodiment, the FCTRX protein is a protein that comprises an amino acid sequence at least about 45% homologous to the amino acid sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the FCTRX proteins of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

Determining Homology Between Two or More Sequences

To determine the percent homology of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are homologous at that position (i.e., as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity").

The nucleic acid sequence homology may be determined as the degree of identity between two sequences. The homology may be determined using computer programs known in the art, such as GAP software provided in the GCG program package. *See*, Needleman and Wunsch, 1970. *J Mol Biol* 48: 443-453. Using GCG GAP software with the following settings for nucleic acid sequence comparison: GAP creation penalty of 5.0 and GAP extension penalty

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of 0.3, the coding region of the analogous nucleic acid sequences referred to above exhibits a degree of identity preferably of at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99%, with the CDS (encoding) part of the DNA sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

The term "sequence identity" refers to the degree to which two polynucleotide or polypeptide sequences are identical on a residue-by-residue basis over a particular region of comparison. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over that region of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, U, or I, in the case of nucleic acids) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the region of comparison (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The term "substantial identity" as used herein denotes a characteristic of a polynucleotide sequence, wherein the polynucleotide comprises a sequence that has at least 80 percent sequence identity, preferably at least 85 percent identity and often 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison region.

### Chimeric and Fusion Proteins

The invention also provides FCTRX chimeric or fusion proteins. As used herein, an FCTRX "chimeric protein" or "fusion protein" comprises an FCTRX polypeptide operativelylinked to a non-FCTRX polypeptide. An "FCTRX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to an FCTRX protein (SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25), whereas a "non-FCTRX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein that is not substantially homologous to the FCTRX protein, e.g., a protein that is different from the FCTRX protein and that is derived from the same or a different organism. Within an FCTRX fusion protein the FCTRX polypeptide can correspond to all or a portion of an FCTRX protein. In one embodiment, an FCTRX fusion protein comprises at least one biologically-active portion of an FCTRX protein. In another embodiment, an FCTRX fusion protein comprises at least two biologically-active portions of an FCTRX protein. In yet another embodiment, an FCTRX fusion protein comprises at least three biologically-active portions of an FCTRX protein. Within the fusion protein, the term "operatively-linked" is intended to indicate that the FCTRX polypeptide and the non-FCTRX polypeptide are fused in-frame with one another. The non-FCTRX polypeptide can be fused to the N-terminus or C-terminus of the FCTRX polypeptide.

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In one embodiment, the fusion protein is a GST-FCTRX fusion protein in which the FCTRX sequences are fused to the C-terminus of the GST (glutathione S-transferase) sequences. Such fusion proteins can facilitate the purification of recombinant FCTRX polypeptides.

In another embodiment, the fusion protein is an FCTRX protein containing a heterologous signal sequence at its N-terminus. In certain host cells (e.g., mammalian host cells), expression and/or secretion of FCTRX can be increased through use of a heterologous signal sequence.

In yet another embodiment, the fusion protein is an FCTRX-immunoglobulin fusion protein in which the FCTRX sequences are fused to sequences derived from a member of the immunoglobulin protein family. The FCTRX-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between an FCTRX ligand and an FCTRX protein on the surface of a cell, to thereby suppress FCTRX-mediated signal transduction in vivo. The FCTRX-immunoglobulin fusion proteins can be used to affect the bioavailability of an FCTRX cognate ligand. Inhibition of the FCTRX ligand/FCTRX interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, as well as modulating (e.g. promoting or inhibiting) cell survival. Moreover, the FCTRX-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-FCTRX antibodies in a subject, to purify FCTRX ligands, and in screening assays to identify molecules that inhibit the interaction of FCTRX with an FCTRX ligand.

An FCTRX chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, e.g., by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., Ausubel, et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An FCTRX-encoding nucleic acid

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can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the FCTRX protein.

FCTRX Agonists and Antagonists

The invention also pertains to variants of the FCTRX proteins that function as either FCTRX agonists (i.e., mimetics) or as FCTRX antagonists. Variants of the FCTRX protein can be generated by mutagenesis (e.g., discrete point mutation or truncation of the FCTRX protein). An agonist of the FCTRX protein can retain substantially the same, or a subset of, the biological activities of the naturally occurring form of the FCTRX protein. An antagonist of the FCTRX protein can inhibit one or more of the activities of the naturally occurring form of the FCTRX protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the FCTRX protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the FCTRX proteins.

Variants of the FCTRX proteins that function as either FCTRX agonists (i.e., mimetics) or as FCTRX antagonists can be identified by screening combinatorial libraries of mutants (e.g., truncation mutants) of the FCTRX proteins for FCTRX protein agonist or antagonist activity. In one embodiment, a variegated library of FCTRX variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of FCTRX variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential FCTRX sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of FCTRX sequences therein. There are a variety of methods which can be used to produce libraries of potential FCTRX variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential FCTRX sequences. Methods for synthesizing degenerate oligonucleotides are well-known within the art. See, e.g., Narang, 1983. Tetrahedron 39: 3; Itakura, et al., 1984. Annu. Rev. Biochem. 53: 323; Itakura, et al., 1984. Science 198: 1056; Ike, et al., 1983. Nucl. Acids Res. 11: 477.

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### Polypeptide Libraries

In addition, libraries of fragments of the FCTRX protein coding sequences can be used to generate a variegated population of FCTRX fragments for screening and subsequent selection of variants of an FCTRX protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of an FCTRX coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S<sub>1</sub> nuclease, and ligating the resulting fragment library into an expression vector. By this method, expression libraries can be derived which encodes N-terminal and internal fragments of various sizes of the FCTRX proteins.

Various techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of FCTRX proteins. The most widely used techniques, which are amenable to high throughput analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique that enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify FCTRX variants. See, e.g., Arkin and Yourvan, 1992. Proc. Natl. Acad. Sci. USA 89: 7811-7815; Delgrave, et al., 1993. Protein *Engineering* 6:327-331.

### **Anti-FCTRX Antibodies**

The invention encompasses antibodies and antibody fragments, such as  $F_{ab}$  or  $(F_{ab})_2$ , that bind immunospecifically to any of the FCTRX polypeptides of said invention.

An isolated FCTRX protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind to FCTRX polypeptides using standard techniques for polyclonal and monoclonal antibody preparation. The full-length FCTRX proteins can be used or, alternatively, the invention provides antigenic peptide fragments of FCTRX proteins for use as immunogens. The antigenic FCTRX peptides comprises at least 4 amino acid residues of the amino acid sequence shown in SEQ ID NO NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and

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encompasses an epitope of FCTRX such that an antibody raised against the peptide forms a specific immune complex with FCTRX. Preferably, the antigenic peptide comprises at least 6, 8, 10, 15, 20, or 30 amino acid residues. Longer antigenic peptides are sometimes preferable over shorter antigenic peptides, depending on use and according to methods well known to someone skilled in the art.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of FCTRX that is located on the surface of the protein (e.g., a hydrophilic region). As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation (see, e.g., Hopp and Woods, 1981. Proc. Nat. Acad. Sci. USA 78: 3824-3828; Kyte and Doolittle, 1982. J. Mol. Biol. 157: 105-142, each incorporated herein by reference in their entirety).

As disclosed herein, FCTRX protein sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or derivatives, fragments, analogs or homologs thereof, may be utilized as immunogens in the generation of antibodies that immunospecifically-bind these protein components. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically-active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that specifically-binds (immunoreacts with) an antigen, such as FCTRX. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain,  $F_{ab}$  and  $F_{(ab')2}$  fragments, and an  $F_{ab}$  expression library. In a specific embodiment, antibodies to human FCTRX proteins are disclosed. Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies to an FCTRX protein sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or a derivative, fragment, analog or homolog thereof. Some of these proteins are discussed below.

For the production of polyclonal antibodies, various suitable host animals (e.g., rabbit, goat, mouse or other mammal) may be immunized by injection with the native protein, or a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed FCTRX protein or a chemicallysynthesized FCTRX polypeptide. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (e.g., aluminum hydroxide), surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), human adjuvants such as Bacille Calmette-Guerin and Corynebacterium parvum, or similar

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immunostimulatory agents. If desired, the antibody molecules directed against FCTRX can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as protein A chromatography to obtain the IgG fraction.

The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of FCTRX. A monoclonal antibody composition thus typically displays a single binding affinity for a particular FCTRX protein with which it immunoreacts. For preparation of monoclonal antibodies directed towards a particular FCTRX protein, or derivatives, fragments, analogs or homologs thereof, any technique that provides for the production of antibody molecules by continuous cell line culture may be utilized. Such techniques include, but are not limited to, the hybridoma technique (see, e.g., Kohler & Milstein, 1975. Nature 256: 495-497); the trioma technique; the human B-cell hybridoma technique (see, e.g., Kozbor, et al., 1983. Immunol. Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see, e.g., Cole, et al., 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the invention and may be produced by using human hybridomas (see, e.g., Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see, e.g., Cole, et al., 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Each of the above citations is incorporated herein by reference in their entirety.

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an FCTRX protein (see, e.g., U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of Fab expression libraries (see, e.g., Huse, et al., 1989. Science 246: 1275-1281) to allow rapid and effective identification of monoclonal Fab fragments with the desired specificity for an FCTRX protein or derivatives, fragments, analogs or homologs thereof. Non-human antibodies can be "humanized" by techniques well known in the art. See, e.g., U.S. Patent No. 5,225,539. Antibody fragments that contain the idiotypes to an FCTRX protein may be produced by techniques known in the art including, but not limited to: (i) an F<sub>(ab')2</sub> fragment produced by pepsin digestion of an antibody molecule; (ii) an F<sub>ab</sub> fragment generated by reducing the disulfide bridges of an  $F_{(ab)2}$  fragment; (iii) an  $F_{ab}$  fragment generated by the treatment of the antibody molecule with papain and a reducing agent; and (iv)  $F_v$ fragments.

Additionally, recombinant anti-FCTRX antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made

> 142 15966-697

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using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in International Application No. PCT/US86/02269; European Patent Application No. 184,187; European Patent Application No. 171,496; European Patent Application No. 173,494; PCT International Publication No. WO 86/01533; U.S. Patent No. 4,816,567; U.S. Pat. No. 5,225,539; European Patent Application No. 125,023; Better, et al., 1988. Science 240: 1041-1043; Liu, et al., 1987. Proc. Natl. Acad. Sci. USA 84: 3439-3443; Liu, et al., 1987. J. Immunol. 139: 3521-3526; Sun, et al., 1987. Proc. Natl. Acad. Sci. USA 84: 214-218; Nishimura, et al., 1987. Cancer Res. 47: 999-1005; Wood, et al., 1985. Nature 314:446-449; Shaw, et al., 1988. J. Natl. Cancer Inst. 80: 1553-1559); Morrison(1985) Science 229:1202-1207; Oi, et al. (1986) BioTechniques 4:214; Jones, et al., 1986. Nature 321: 552-525; Verhoeyan, et al., 1988. Science 239: 1534; and Beidler, et al., 1988. J. Immunol. 141: 4053-4060. Each of the above citations are incorporated herein by reference in their entirety.

In one embodiment, methods for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and other immunologically-mediated techniques known within the art. In a specific embodiment, selection of antibodies that are specific to a particular domain of an FCTRX protein is facilitated by generation of hybridomas that bind to the fragment of an FCTRX protein possessing such a domain. Thus, antibodies that are specific for a desired domain within an FCTRX protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

Anti-FCTRX antibodies may be used in methods known within the art relating to the localization and/or quantitation of an FCTRX protein (e.g., for use in measuring levels of the FCTRX protein within appropriate physiological samples, for use in diagnostic methods, for use in imaging the protein, and the like). In a given embodiment, antibodies for FCTRX proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody derived binding domain, are utilized as pharmacologically-active compounds (hereinafter "Therapeutics").

An anti-FCTRX antibody (e.g., monoclonal antibody) can be used to isolate an FCTRX polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-FCTRX antibody can facilitate the purification of natural FCTRX polypeptide from cells and of recombinantly-produced FCTRX polypeptide expressed in host cells. Moreover, an anti-FCTRX antibody can be used to detect FCTRX protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the FCTRX protein. Anti-FCTRX antibodies can be used diagnostically to monitor protein levels in tissue as part of a

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clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include <sup>125</sup>I, <sup>131</sup>I, <sup>35</sup>S or <sup>3</sup>H.

## FCTRX Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an FCTRX protein, or derivatives, fragments, analogs or homologs thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively-linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis